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Biol. Chem. Hoppe-Seyler, Vol. 376, June, 1995, pages 385 to 388 Biosci. Biotech. Biochem., Vol. 57, No. 9, 1993, pages 1470 to 1476 Febs letters, Vol. 336, No. 3, 1993, pages 555 to 559 Journal of Chromatography, Vol. 568, No. 1, 1991, pages 55 to 68 Comp. Biochem. Physiol., Vol 96B, No. 2, 1990, pages 247 to 252 J. Biochem., Vol. 87, No. 4, 1980, pages 1133 to 1143

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(54) Production and purification of cathepsin L for X-ray crystallography

(57) Cathepsin L is a thiol protease and produced by cloning human epithelial cell DNA into E. coli using a secretion vector. The proenzyme is secreted into the periplasmic space of the E. coli and purified to a high specific activity (at least 40.000 nmoles/min/mg). The purified, correctly folded enzyme was crystallised and X-ray coordinates determined for use in rational drug design.

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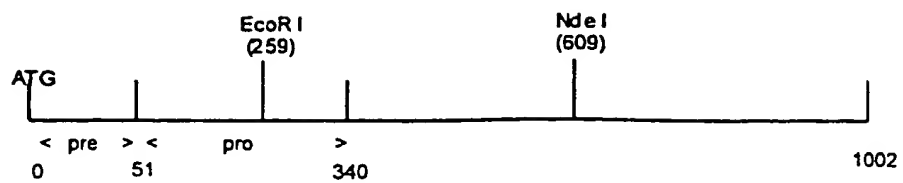
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Figure 1

preproCathepsin L

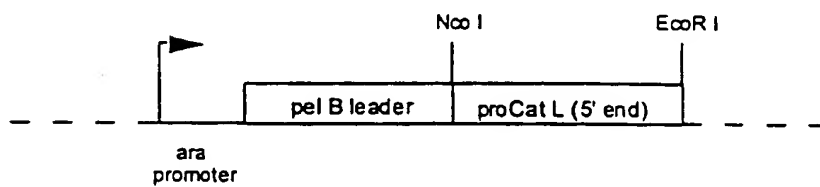
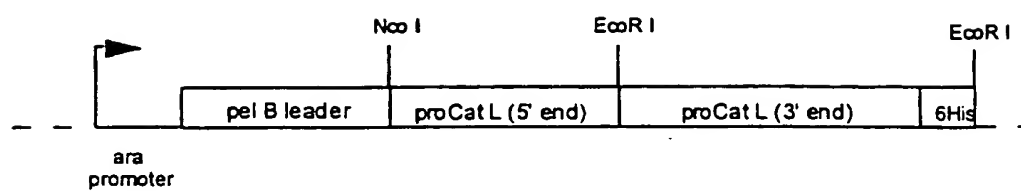
Figure 2**Figure 3**

Figure 4

pDP 483

PROTEIN

The present invention relates to cathepsin L in biologically active form, methods of making cathepsin L in *E. coli*, cathepsin L in crystalline form, use of the X-ray structure
5 atomic co-ordinates in rational drug design and drugs obtained thereby.

Cathepsin L is a thiol protease that plays an important role in the degradation of proteins within the lysosomes and in the extracellular matrix. It occurs in at least three forms: prepro-; pro- and; mature cathepsin L. Furthermore, mature cathepsin L can be "clipped" through proteolysis to yield heavy and light chains. The pro and prepro forms are
10 biologically inactive.

Besides its role in protein turnover, cathepsin L has been implicated in bone remodelling, glomerulonephritis, rheumatoid arthritis, antigen processing and tumour metastasis. The search for drugs that intervene in these diseases has been impeded by lack of knowledge as to the three-dimensional structural determinants of the specificity of
15 cathepsin L. These can only be accurately ascertained through the technique of X-ray crystallography, which involves the analysis of X-ray diffraction of a crystalline sample.

Obtaining a crystalline sample suitable for the structural analysis of cathepsin L has eluded all researchers to date. The supply of pure active protein for crystallisation trials has been a major stumbling block in the growth of large crystals. Whilst not wishing to be
20 bound by theoretical considerations the presence of a free cysteine residue at the active site (which can cause mis-matched disulphide bond pairing) probably contributes to making the folding process complex. The sensitivity of the enzyme to extremes of pH also makes the enzyme difficult to handle because it is often desirable to work with the enzyme at extremes of pH such as for example in refolding experiments.

25 Abbreviations:

CM	carboxymethyl
dOT	dissolved oxygen tension
NHMec	7-amido-4-methyl-coumarin
MPD	methylpentandiol
30 NTA	nitrilo-triacetic acid
OTR	oxygen transfer rate

OUR	oxygen uptake rate
PAGE	polyacrylamide gel electrophoresis
PCR	polymerase chain reaction
SDS	sodium dodecyl sulphate
5 VVM	volume volume per minute
Z	benzyloxycarbonyl

In an early report Smith and Gottesman (1989) in *J. Biol. Chem.* 264: 20487-20495, described the expression of human procathepsin L in *E. coli* as an insoluble product in inclusion bodies. They described the isolation and subsequent solubilisation of inclusion
10 bodies followed by folding then activation (by acid treatment) of the enzyme to produce active enzyme in poor yield (<1% by activity). The authors reported that the majority of the product in the renaturation extract was insoluble and by implication misfolded. After purification by Sephadex G-75 chromatography the specific activity (as measured by the Z-Phe-Arg-NHMec assay described below) of the purified folded product was low (22,000
15 nmol/min/mg) implying that only a portion of the final pure product was in the correctly folded state.

Dolinar et al ((1995) *Biol. Chem. Hoppe-Seyler*, 376: 385-388) have also described the expression of procathepsin L in *E. coli* as an insoluble product in inclusion bodies, followed by extraction and solubilisation of the inclusion bodies then folding of
20 procathepsin L followed by acid activation. Despite improvements in yield to 4.4%, the authors calculate that only 30% of their folded cathepsin L product is active, implying that 70% of the product is inactive, presumably still misfolded. The misfolded enzyme would act to frustrate the crystallisation of the enzyme as the misfolded enzyme would interfere with the build up of ordered arrays of molecules that constitute the formation of the crystal.

25 The present invention is based on overcoming several technical hurdles: (1) we have secreted procathepsin L into *E. coli* periplasm in soluble form; (2) we have purified active cathepsin L from the growth medium in milligram amounts at high specific activity >100,000 nmoles/min/mg; (3) we have devised a process for the production of correctly folded molecules from soluble incorrectly folded molecules; (4) we have obtained
30 cathepsin L in a crystalline form; (5) collected an X-ray diffraction data set from the crystals and; (6) we have determined the 3-dimensional structure of cathepsin L from the

X-ray diffraction data. This involved using papain as a model in molecular replacement procedures. The structure has been refined to give an accurate model which is used to understand the enzyme specificity and forms the basis of rational drug design.

According to one aspect of the present invention there is provided protein cathepsin L in which at least 40 % of the protein is correctly folded in a biologically active conformation. Preferably at least 50 % of the protein is correctly folded, more preferably at least 60 % of the protein is correctly folded, more preferably at least 70 % of the protein is correctly folded, more preferably at least 80 % of the protein is correctly folded, more preferably at least 90 % of the protein is correctly folded and especially at least 95 % of the protein is correctly folded.

The term "cathepsin L" as used herein (unless otherwise apparent from the context used) includes analogues or variants such as for example cathepsin L - (His)₆ where the (His)₆ tag is used to assist purification but other analogues are contemplated especially conservative analogues which would not unduly alter the biological properties of the protein. Generally cathepsin L is in isolated form meaning it is at least partially purified from its naturally occurring state.

The terms "Cathepsin L-6His" and "cathepsin L - (His)₆" refer to cathepsin L with a tag of 6 histidine amino acids added to its C-terminus.

According to another aspect of the present invention there is provided cathepsin L at a specific activity of at least 40,000 nmoles/min/mg. Specific activity is determined using the Z-Phe-Arg-NHMec assay described below. Preferably the specific activity is at least 50,000 nmoles/min/mg, more preferably the specific activity is at least 60,000 nmoles/min/mg, more preferably the specific activity is at least 70,000 nmoles/min/mg, more preferably the specific activity is at least 80,000 nmoles/min/mg, more preferably the specific activity is at least 90,000 nmoles/min/mg and especially the specific activity is at least 100,000 nmoles/min/mg.

According to another aspect of the present invention there is provided a method of making cathepsin L which comprises directed expression of procathepsin L encoded on an expression vector into the periplasm of *E.coli* cultured in a growth medium. Preferably the *E.coli* is cultured at a temperature of 15-30°C and especially at 25°C. Preferably the expression vector comprises inducible expression control and the growth medium

comprises a concentration of inducer optimised for maximal soluble expression of cathepsin (this is a lower concentration, optimised for example by titration, than the concentration of inducer required for maximal expression of cathepsin). Culture of *E.coli* at low temperature (15-30°C) gives a slow rate of cathepsin production which has the advantage of producing higher yields of correctly folded soluble cathepsin; use of a low concentration of inducer enhances this advantageous effect. Preferably soluble cathepsin L is collected from growth medium and activated by removal of the pro sequence and clipping the cathepsin into its 2-chain form..

According to another aspect of the present invention there is provided a secretion vector for directed expression of cathepsin L into the periplasm of *E.coli*.

According to another aspect of the present invention there is provided an *E.coli* host comprising a secretion vector for directed expression of procathepsin L into the host periplasm.

According to another aspect of the present invention there is provided *E. coli* MSD 2148 (MSD 213 pZen 1677) deposited under the Budapest Treaty as NCIMB accession no 40773 on 11th October 1995 with the National Collection of Industrial & Marine Bacteria, 23 St Machar Drive, Aberdeen AB2 1RY, Scotland, United Kingdom.

According to another aspect of the present invention there is provided cathepsin L in crystalline form. Preferably the crystals possess a monoclinic space group $P2_1$, with unit cell dimensions $a = 46.23$, $b = 49.38$, $c = 49.25$ Å and $\beta = 113.45^\circ$. Preferably the crystals are wedge-shaped crystals and are preferably about 0.1 mm^3 . Preferably the crystals essentially have the atomic coordinates set out in Example 4.

According to another aspect of the present invention there is provided X-ray coordinates of cathepsin L. Preferably the coordinates are substantially as set out in Example 4. Preferred X-ray coordinates are of the active site of cathepsin L as defined in Example 4 in residues 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189 & 209-214.

According to another aspect of the present invention there is provided the use of the 3-dimensional structure of cathepsin L as determined from X-ray diffraction data in rational drug design. Preferred methods are described in Example 3 such as any of the following:

searching real and virtual compound databases for potential drugs; computational growth of ligands in the active site; and collecting X-ray diffraction data from crystals comprising potential drug.

According to another aspect of the present invention there is provided a novel
5 inhibitor of cathepsin L determined by rational drug design using X-ray diffraction data of cathepsin L. The cathepsin L catalytic residues, ie those who play an active role in catalysis,
are Cys25, His163, Gln19, Asn183, and, in a structural role, Trp185. This however,
is a configuration conserved in almost all cysteine proteases, and we need to look beyond
10 the active site when carrying out drug design specific to cathepsin L. In fact, the surface of the entire active site cleft can be important. The following residue ranges form the active site cleft and therefore are most likely to be involved in drug design: 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189, 209-214. Note that any one drug would only interact with a subset of these.

15 The invention will now be illustrated by the following non-limiting examples in which:

SEQ ID NO: 7 illustrates a cDNA nucleotide sequence of cathepsin L in which 289-339 represents signal peptide, 289-1290 represents pro-cathepsin L and, 340-1290 represents mature cathepsin L (Gal S. 1988, Biochem. J. 253, 303-306);

20 SEQ ID NO: 8 illustrates an amino acid sequence of cathepsin L in which 1-17 represents signal peptide, 18-113 represents pro peptide, 114-288 represents heavy chain and 292-333 represents light chain (Ritonja 1988, FEBS Letters 228, 341-345; Mason 1986, Biochem. J. 240, 373-377; Joseph 1987, Nucleic Acids Research 15, 3186) and;

Figure 1 illustrates a cloned PCR product showing restriction sites;

25 Figure 2 illustrates pDP480;

Figure 3 illustrates pCRII/cathepsin L-6-His and;

Figure 4 illustrates pDP483 (pZEN1677).

Example 1 - Production of recombinant human cathepsin L-6His

1.1 Cloning of Cathepsin L-6His

The coding sequence for full length preprocathepsin L was generated from a human epithelial cell cDNA library by PCR using oligonucleotides complementary to the 5' and 3'

5 ends:

5' - 3' Oligonucleotide:

GCAGTAAGATATGAATCCTACACT (SEQ ID NO: 1)

3' -5' Oligonucleotide: (listed 5' - 3')

CATCACCGTCCACAGCTCACACAG (SEQ ID NO: 2)

10

The PCR product generated was cloned into the PCR cloning vector pCR II (Invitrogen). A diagram of the cloned PCR product showing relevant restriction sites is shown in Figure 1. This construct formed the starting material for generation of the *E.coli* secretion vector construct.

15 1.2 Generation of *E.coli* procathepsin L-6His secretion vector

The vector used for secretion of Cathepsin L in *E.coli* was pAG170.

In pAG170, sequences to be expressed are cloned downstream of the *Erwinia carotovora* pel B secretory leader sequence under control of the ara B/C promoter from *Salmonella typhimurium*.

20

For cloning into pAG170, a PCR product was generated incorporating the sequence from the start of the pro region to the internal EcoR I site of procathepsin L, using the initial Cathepsin L construct above as the target DNA. The 5'-3' oligonucleotide also introduced a Nco I restriction site. The 3'-5' oligonucleotide was complementary to sequence encompassing the internal EcoR I site.

25

5'-3'oligonucleotide:

Nco I

GATGACCATGGCGACTCTAACATTTGATCACAG (SEQ ID NO: 3)

30 3'-5' oligonucleotide:

EcoR I

CTGCCTGAATTCCTTCACTGGTCATGTCTC (SEQ ID NO: 4)

The PCR product generated was digested with Nco I and EcoR I and cloned into Nco I / EcoR I digested pAG170. A clone with correct sequence was identified (as pDP 5 480) and is shown diagrammatically in Figure 2. The 3' end of procathepsin L from an internal Nde I site to the end of the coding sequence was then generated by PCR. The 5' - 3' oligonucleotide encompassed the internal Nde I site. The 3' - 5' oligonucleotide was designed so as to introduce a 6 histidine residues (for purification purposes) immediately upstream of the translational stop codon as well as EcoR I and Hind III restriction sites 10 downstream of the coding sequence.

5' - 3' Oligonucleotide:

Nde I

CTATCCATATGAGGCAACAGAAGAATCCTG (SEQ ID NO: 5)

15

3' - 5' Oligonucleotide:

Hind III EcoR I stop codons 6 His tag

GACAAGCTT GAATTC TTA TTA GTGATGGTGATGGTGGTG
CACAGTGGGGTAGCTGGCTG (SEQ ID NO: 6)

20

The PCR product obtained was digested with Nde I and Hind III and cloned back into Nde I / Hind III digested pCR II preprocathepsin L to replace original sequence. The sequence of the 6-His tagged 3' Nde I - EcoRI fragment was confirmed (including sequence upstream of the Nde I site). A diagram of pCRII/Cathepsin L-6His is shown in 25 Figure 3.

To complete the cloning of procathepsin L into the secretion vector, the fragment of procathepsin L-6His from the internal EcoR I site to the EcoR I site at the 3' end was excised from the pCR II construct and cloned into EcoR I digested pDP480. A clone of the correct orientation was identified. This generates a tetracycline resistant plasmid encoding 30 procathepsin L-6His downstream of an in-frame pel B secretion leader, whose expression is under the control of an ara B/C promoter / regulator cassette. This construct was initially

designated pDP 483 and is shown diagrammatically in Figure 4. The construct was designated pZen 1677 (also known as pCI 1677; NCIMB 40773).

1.3 Fermentation process for procathepsin L-6His

E.coli strain MSD 213 was transformed with plasmid pZen 1677 and the resultant strain MSD 2148 (MSD 213 pZen 1677; NCIMB No 40773) stored as a glycerol stock at -80°C. An aliquot of MSD 213 pZen 1677 was streaked onto agar plates of L-tetracycline to separate single colonies after overnight growth at 37°C. A single colony of MSD 213 pZen 1677 was removed and resuspended in a 10ml L-tetracycline broth and 100µl immediately inoculated into each of seven 250ml Erlenmeyer flasks containing 75ml of L-tetracycline broth. After growth for 15h at 37°C on a reciprocating shaker the contents of the flasks were pooled and used to inoculate a single fermenter containing 15L of the growth medium described in the Table below.

Table - Growth medium

Component	Concentration g/L deionized water
Potassium dihydrogen orthophosphate	3.0
di-Sodium hydrogen orthophosphate	6.0
Sodium chloride	0.5
Casein hydrolysate (Oxoid L.41)	2.0
Ammonium sulphate	10.0
Glycerol	35.0
Yeast Extract (Difco)	20.0
Magnesium sulphate 7-hydrate	0.5
Calcium chloride 2-hydrate	0.03
Thiamine	0.008
Iron sulphate 7-hydrate/Citric acid	0.04/0.02
Trace element solution (TES)*	0.5ml/L
Tetracycline	(10mg/L)

*Trace metal solution (TES)

Component	mg/10ml deionized water
$\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$	2.0
$\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$	0.8
$\text{KCr}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$	0.2
$\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$	0.2
H_3BO_3	0.1
KI	2.0
$\text{MnSO}_4 \cdot \text{H}_2\text{O}$	2.0
$\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$	0.09
$\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$	0.4
$\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.4

The fermentation was carried out at a temperature of 37°C and pH, controlled by automatic addition of 6M sodium hydroxide and 2M sulphuric acid solutions, of pH 6.7.

5 The dissolved oxygen tension (dOT) set-point was 50% air saturation and was controlled by automatic adjustment of the fermenter stirrer speed. Air flow to the fermenter was 20L/min corresponding to 1.33 volume volume per minute (VVM). A solution of yeast extract (stock 900g/4L) was fed into the fermenter at a rate of 190ml/h from 4,5h post inoculation. When the culture OD₅₅₀ reached ca. 40-45 (6h post inoculation), the

10 fermentation temperature was decreased to 25°C and the fermentation continued at this temperature under the conditions described above for a further 1h.

When the culture OD₅₅₀ reached ca. 50-55 (7h post inoculation) procathepsin L-6His expression/secretion was induced by adding 75g L-arabinose to the fermenter (150ml of 50% stock). The fermentation was continued under these conditions until the supply of

15 carbon source (glycerol) in the fermentation became exhausted (9h post inoculation) leading to a rapid rise in the dOT from 50% air saturation. At this point, a feed containing glycerol (714 g/L) and ammonium sulphate (143 g/L) was fed pumped into the fermenter. The rate at which this feed was supplied was adjusted to restrict the bacterial oxygen uptake rate (OUR) to approximately 80% of the fermenters maximum oxygen transfer rate

20 (OTR), under the conditions described, whilst first returning and then maintaining the dOT at 50% air saturation. The fermentation was continued under these conditions until about

56h post fermenter inoculation when the culture was harvested by transferring aliquots of the fermenter contents into 1L centrifuge bottles.

The spent medium was separated from the bacterial cells by centrifugation in a Sorvall™ RC-3B centrifuge (7000x g, 4°C, 30min). Accumulation of procathepsin L-6His in the spent growth medium, and periplasm (extracts prepared using osmotic shock) was determined using SDS-PAGE followed by western blotting using an anti-Cathepsin L antibody as the primary antibody.

1.4 Purification of cathepsin L-6His

E. coli broth (MSD 2148; NCIMB no 40773) was harvested by centrifugation at 5000 rpm for 30 min in a H 6000A rotor (Sorvall Instruments). All procedures were carried out at 4°C except where stated. The pellet was discarded while the supernatant (10 litres) was concentrated to 1 litre and dialysed with 15 litres of 20 mM Tris.HCl pH 7.0 in a spiral cartridge (Amicon™). The retentate was centrifuged at 12,000 rpm for 30 min in a GSA™ rotor (Sorvall Instruments). The pellet was discarded and the supernatant was further centrifuged for 35,000 rpm for 30 min in a 45 Ti rotor (Beckman Instruments).

The pellet was discarded and the supernatant was applied to a 1.5 cm x 3 cm Ni²⁺ Nitrilo-tri-acetic acid-agarose column (QiaGen™) (flow rate 1 ml/min) equilibrated with 20 mM Tris.HCl pH 7.0. The unbound protein was collected and applied to a second 1.5 cm x 11 cm NTA column equilibrated with the the above buffer. Both columns were washed with 20 mM Tris.HCl pH 7.0, followed by 300 mM NaCl, 20 mM Tris.HCl pH 7.0, then 300 mM NaCl, sodium acetate pH 6.0 and finally eluted with 500 mM imidazole, sodium acetate pH 6.0. The two eluates (final pH 6.3) were pooled (protein concentration 1.3 mg/ml) and dialysed against 3 x 5 litres 20 mM sodium acetate pH 5.8 over 72 h. As a precipitate formed on dialysis, the combined eluates were centrifuged at 35,000 rpm for 30 min in a 45 Ti rotor™ (Beckman). The pellet (P) fraction was collected (note this material resulted in the isolation of cathepsin L-6His which surprisingly *could* be crystallised whilst cathepsin from the soluble fraction could not).

The P fraction was resuspended in 20 mM Tris.HCl pH 7.0, incubated for 48 h, spun at 35,000 rpm for 30 min in a 45 Ti rotor™ and then treated at pH 4 for 60 min at 22°C. The solution was subsequently dialysed against 20 mM sodium acetate pH 5.5. The dialysate was applied to an ion exchange column (CM Fractogel™ (E. Merck/BDH),

1.5 cm x 11 cm, flow rate 1.0 ml/min) equilibrated with 20 mM sodium acetate pH 5.5, washed with 20 mM sodium acetate pH 5.5 and eluted with a gradient of 0-500 mM sodium chloride in 20 mM sodium acetate pH 5.5. The fractions were assayed using a Z-Phe-Arg-NHMec assay and the active fractions were pooled and subsequently treated at pH 5.4 for 60 min at 22°C. The pool was frozen at -20°C.

Samples were thawed to 4°C and dialysed against sodium acetate pH 4.4 (3 x 5 litres) overnight and finally stored at -20°C.

1.5 Z-Phe-Arg-NHMec assay for cathepsin L-6His

Cathepsin L-6His protein was incubated at 37°C for 30 min with the substrate 20 µM Z-Phe-Arg-NHMec in an incubation buffer (total incubation volume = 175 µl). The reaction was stopped with 175 µl stop buffer. The sample was excited at 370 nm, and the emitted fluorescence was measured at 460 nm. Incubation buffer comprises: 88 mM KH₂PO₄, 12 mM Na₂HPO₄, 1 mM EDTA (disodium salt), 0.1% Brij 35 and 1 mM cysteine. Stop buffer comprises: 5.75 ml glacial acetic acid and, 11.6 g sodium chloracetate per litre water adjusted pH to 4.3 with NaOH. Results are expressed as nmoles of product formed per min normalised per mg of protein present (as measured by the Bradford method).

Example 2 - Crystallisation and Structure Determination

This work was performed on mature "clipped" cathepsin L i.e. in two-chain form, 175 amino acids and 42 amino acids, linked by a disulfide bridge with 3 residues being chopped off when the mature form was clipped.

Samples of purified cathepsin L (from Example 1.4) were thawed and concentrated on a Centricon C-10™ centrifuge filtration device (Amicon) using a GA-10 rotor™ operating at 5000 rpm at 10°C until final protein concentration as determined by Bradford method was 10 mg/ml. No crystals resulted, but initial indications for probable crystallisation conditions were found using the commercially available Hampton™ screening conditions (Jancarik, J & Kim, S.H. J. Appl. Cryst. 1991, 24, 409-411) on a Douglas Instruments Impax V™ crystallisation robot, which prepares small drops under oil using the batch crystallisation method (McPherson, A. 1982. *Preparation and analysis of protein crystals*. John Wiley & Sons, New York). Crystallisation conditions were then found and optimised manually using trays of hanging drop vapour diffusion experiments

(McPherson, A. 1982. *Preparation and analysis of protein crystals*. John Wiley & Sons, New York). Best results were obtained when 4 μL of protein solution were dispensed onto siliclad coverslips and carefully mixed with an equal volume of reservoir solution (100mM cacodylate buffer at pH6.2 containing 30% 2-methylpentan-2,4-diol). The coverslips were
5 inverted and the drop were suspended over wells containing 950 μL of reservoir solution. The hanging drop experiments were equilibrated at 4°C. Wedge-shaped crystals appeared after 2-4 days and grew to their full size, typically 0.1 mm^3 , within 7 days.

2.1 Data collection and processing

The crystallisation conditions fortuitously also functioned as cryoprotectant since
10 they contained 30% methylpentandiol (MPD). This means the crystals could be flash frozen in a cold nitrogen stream at 100°K using the a cryostream cooler (Oxford Cryosystems™), thereby protecting the crystal against radiation damage, which was considered important given the small size of the crystals. A frozen crystal diffracted X-rays to 2Å resolution. Intensity data were recorded on a 30cm Imaging Plate
15 (MarResearch) positioned 150mm away from the crystal. X-rays were generated by a rotating anode generator (Enraf-Nonius FR571™) operating at 40 kV and 90 mA, producing graphite monochromatised $\text{CuK}\alpha$ X-radiation. Images of 1° of crystal rotation were recorded with 30 minutes exposure. After a number of images were collected, the autoindexing routines in XDS software™ (Kabsch, W. 1988. Acta Cryst A21, 916-924)
20 adapted for use with the MAR image plate were used to determine the symmetry and unit cell dimensions of the crystal. These were consistent with the monoclinic space group $P2_1$, with $a = 46.23$, $b = 49.38$, $c = 49.25$ Å and $\beta = 113.45^\circ$. The presence of a single molecule of cathepsin L in the asymmetric unit corresponds to a volume to mass ratio of $V_M^{-2.1}$ Å³/Da, or a solvent content of about 40% in the crystal. The data collection was continued
25 for 5 days on a single crystal, which would probably not have been possible without freezing the crystal. The 27496 intensity data were merged across equivalent reflections to give 12421 unique reflection intensities using the program MARSCALE. The overall R_{merge} was 6.0% for all data between 15 and 2Å, while in the highest resolution shell (2.4-2.0Å) R_{merge} was 11.9%. The intensity data were reduced to structure amplitudes
30 using the program TRUNCATE in the CCP4 suite (CCP4, 1994, Acta Cryst D50, 760-763).

2.2 Structure solution and refinement

Since there is 40% amino acid identity with papain, a well-refined papain model was thought to be a suitable trial model for molecular replacement. Three variations of the trial model were created: firstly a full papain model (Brookhaven Data Bank entry 9PAP),
5 secondly the papain model with side chains truncated to the least common denominator and insertions with respect to cathepsin L deleted, and thirdly a homology model of cathepsin L built from the papain structure and energy minimised.

The program AMORE as available from the CCP4 suite of protein crystallography programs (CCP4, 1994, Acta Cryst D51, 760-763) was used for the molecular replacement.
10 Structure factors for the trial models were calculated in a cubic cell of 80 Å. The molecular replacement was carried out using all data between the resolution limits 10 and 4 Å within a Patterson integration radius of 25 Å. The three trial models gave Rotation function values of 24, 23 and 21, respectively, which were over twice the value of the next highest peak in the rotation function maps. Following the translation function, the correlation between
15 observed and calculated data were, for the three trial models, 0.395, 0.440 and 0.355 respectively, while the crystallographic R-values were 46.6, 46.0 and 48.8%, for the full papain, trimmed papain, and homology model respectively.

Inspection with computer graphics showed that papain molecules rotated and translated to these molecular replacement solutions packed well into the unit cell without
20 any interpenetration of neighbouring molecules. The full papain and trimmed papain models gave equivalent solutions, while the homology model had positioned the molecule correctly but upside down relative to the papain models. Attempts to refine the homology model solution were not successful. The trimmed papain molecule, rotated and translated from the Brookhaven data bank coordinates (entry 9PAP) by the eulerian angles $\alpha =$
25 235.63° , $\beta = 168.58^\circ$, and $\gamma = 95.75^\circ$ and by the fractional coordinates 0.160166, 0.0, - 0.27854, was taken for further work.

This model was refined using the program XPLOR™ and the standard simulated annealing protocol suggested by Bruenger (Bruenger, 1988, J.Mol. Biol. 203, 803-816).

The refinement used all data between 10 and 2 Å. After the first round of refinement, R was
30 35%, but the R_{free} still around 43%, suggesting considerable model bias. Inspection of a 2Fo-Fc electron density map showed that while part of the model fit the density well there

were also large portions of the molecule where the agreement with the density was poor. However, the solution was undoubtedly correct since exceptionally clear sidechain density for several aromatic amino acid residues was visible where as the model had been truncated to C β in these cases.

5 As much of the electron density was interpreted as possible and those portions where the interpretation was not clear were omitted from the model altogether before refinement continued. The model consisted of 6 segments at the next round of refinement. A second round of simulated annealing refinement using XPLOR™ resulted in R = 37% and R_{free} = 44%, however the electron density map now shows clearly the positions of
10 many side chains and of some of the loops that were previously omitted, although there still remained some 30 residues which have not been built correctly yet. The model was again subjected to simulated annealing resulting in R=34% to 2Å. The resultant electron density map now shows all missing loops. Individual isotropic atomic temperature factors have been applied and solvent water molecules have been added to the model. This results
15 in an accurate structure (2Å) of cathepsin-L. The coordinates of the model are set out in Example 4. This model has R=21% with 157 solvent water molecules included.

Example 3: Use of the cathepsin L structure in structure-based drug design

Having determined the coordinates for the atomic structure of cathepsin L, as well
20 as having devised the crystallisation protocol for cathepsin L, we are now in a strong position to design drugs against the disease targets that involve cathepsin L, such as bone resorption and osteoporosis. The approaches used for this include the following.

(1) We superpose our cathepsin L coordinates onto other available coordinates of thiol proteases which have inhibitors bound to give us a first approximation of the way these and
25 related inhibitors might bind cathepsin. The active site of cathepsin is very similar to that of papain for example, as might be expected from sequence homology. However, inhibitors of papain such as leupeptin extend to a region of the protease where the homology begins to break down, and these different areas in the protein confer different binding modes for the inhibitors which can be modelled. We can see which parts of the
30 inhibitors can be modified without affecting the interactions the inhibitor makes with the protein; it is these modifications that can be used to adjust the physical properties of the

inhibitor without affecting the binding. We can also predict modifications of the inhibitor which lead to stronger interactions with the protein; this is rational optimisation of a lead compound. Such predictions are made in conference with medicinal chemists who assess the feasibility of synthesis - this allows us to generate compounds that can be tested in
5 activity assays and which may be complexed with the cathepsin crystals allowing rapid X-ray determination of the complex structure.

(2) Using our coordinates for the cathepsin L molecule, we use a variety of available ligand design software to generate pharmacophore models that are specific for binding at the cathepsin L active site. These in turn can be used to search real and virtual compound
10 data bases to provide a list of possible candidate inhibitors that match the pharmacophore. Another way to generate models of ligands is to "grow" them in the active site. The software used includes commercially available programs such as LUDI™ and LEAPFROG™.

LUDI™ examines interactions of molecular fragments from a data base with the
15 protein active site, and allows the user to build up a chemically realistic molecule from suitable fragments.

LEAPFROG™ "grows" new ligands using a genetic algorithm, the parameters that direct the growth of the ligand being under the control of the user.

Compounds proposed by the ligand design software are synthesised and tested for
20 activity. If active, they can be complexed with crystals of cathepsin L for structural analysis.

(3) An important step in the drug design cycle is the feedback of how a designed compound truly interacts with the protein, which can be done if a crystallisation protocol is in place. The crystals can be soaked in a solution of the inhibitor for 24 hours before
25 collecting the X-ray diffraction patterns. A (complex-native) difference Fourier synthesis using the phases derived from the native protein crystal structure is a straight forward calculation which rapidly gives the electron density at atomic resolution for the inhibitor, showing exactly where and how it binds. Alternatively, the crystals can be grown in the presence of the inhibitor. The crystal structure of the inhibitor complex is useful in many
30 ways, for example, it allows us to examine unambiguously the interactions that the inhibitor makes with the protein so that we can enter a new cycle of rational improvement,

and it also enables us to identify parts of the molecule which may be modified in order to alter physical properties without compromising binding in order to improve *in vivo* activity. Importantly, it allows us to learn how well our intended optimisations resemble what actually occurs in the crystal, so that we may refine further our own ability to design

5 optimised inhibitor-protein interactions.

(4) Inhibitors found by random screening can be optimised rationally as in (3).

(5) The inhibitors found from two different chemical series by any of the above methods can be combined rationally to produce hybrid compounds that incorporate the protein interactions seen in both series of inhibitors to maximum effect.

10 (6) Inhibitors found using the above methods are analysed structurally to arrive at ways of generating diversity through the use of carefully designed chemical libraries. In this way, larger numbers of substituents can be tested for activity and additional compounds of interest can be optimised further by re-entering them in the rational design cycle.

Inhibitors identified using the above methods are analysed further in assays
15 including *in vivo* assays.

Example 4

Coordinates for Cathepsin L

	CRYSTL	46.430	49.380	49.250	90.00	113.45	90.00	1	
20	SCALE1	0.021538	0.000000	0.009343			0.000000		
	SCALE2	0.000000	0.020251	0.000000			0.000000		
	SCALE3	0.000000	0.000000	0.022133			0.000000		
	ATOM	1	CB	ALA A	1	-0.877	21.216	12.640	1.00 27.20
	ATOM	2	C	ALA A	1	-1.316	22.399	10.477	1.00 26.12
25	ATOM	3	O	ALA A	1	-2.175	23.276	10.518	1.00 27.83
	ATOM	4	N	ALA A	1	-0.251	23.588	12.251	1.00 28.44
	ATOM	5	CA	ALA A	1	-0.342	22.242	11.626	1.00 26.83
	ATOM	6	N	PRO A	2	-1.145	21.617	9.400	1.00 23.75
	ATOM	7	CD	PRO A	2	-0.077	20.646	9.107	1.00 22.84
30	ATOM	8	CA	PRO A	2	-2.071	21.736	8.271	1.00 21.66
	ATOM	9	CB	PRO A	2	-1.442	20.821	7.220	1.00 21.82
	ATOM	10	CG	PRO A	2	0.014	20.739	7.623	1.00 22.38
	ATOM	11	C	PRO A	2	-3.447	21.218	8.691	1.00 20.10
	ATOM	12	O	PRO A	2	-3.625	20.729	9.802	1.00 18.59

ATOM	13	N	ARG A	3	-4.436	21.357	7.821	1.00	19.96
ATOM	14	CA	ARG A	3	-5.766	20.857	8.152	1.00	21.14
ATOM	15	CB	ARG A	3	-6.874	21.772	7.577	1.00	24.00
ATOM	16	CG	ARG A	3	-6.892	23.174	8.259	1.00	28.09
5 ATOM	17	CD	ARG A	3	-8.252	23.863	8.215	1.00	30.40
ATOM	18	NE	ARG A	3	-8.696	24.080	6.840	1.00	32.98
ATOM	19	C2	ARG A	3	-9.915	23.796	6.388	1.00	33.51
ATOM	20	NH1	ARG A	3	-10.831	23.280	7.208	1.00	33.09
ATOM	21	NH2	ARG A	3	-10.211	24.009	5.105	1.00	33.81
10 ATOM	22	C	ARG A	3	-5.913	19.387	7.718	1.00	17.20
ATOM	23	O	ARG A	3	-6.685	18.629	8.302	1.00	16.72
ATOM	24	N	SER A	4	-5.125	18.999	6.723	1.00	14.03
ATOM	25	CA	SER A	4	-5.107	17.646	6.197	1.00	11.83
ATOM	26	CB	SER A	4	-5.728	17.601	4.802	1.00	11.68
15 ATOM	27	OG	SER A	4	-7.126	17.827	4.870	1.00	15.44
ATOM	28	C	SER A	4	-3.656	17.219	6.087	1.00	9.98
ATOM	29	O	SER A	4	-2.792	18.029	5.745	1.00	8.83
ATOM	30	N	VAL A	5	-3.387	15.960	6.407	1.00	8.94
ATOM	31	CA	VAL A	5	-2.044	15.402	6.312	1.00	9.62
20 ATOM	32	CB	VAL A	5	-1.311	15.383	7.684	1.00	8.56
ATOM	33	CG1	VAL A	5	-0.101	14.476	7.597	1.00	9.25
ATOM	34	CG2	VAL A	5	-0.860	16.787	8.085	1.00	8.49
ATOM	35	C	VAL A	5	-2.177	13.970	5.823	1.00	9.02
ATOM	36	O	VAL A	5	-3.069	13.257	6.284	1.00	10.58
25 ATOM	37	N	ASP A	6	-1.315	13.573	4.888	1.00	7.29
ATOM	38	CA	ASP A	6	-1.292	12.212	4.348	1.00	7.93
ATOM	39	CB	ASP A	6	-2.235	12.040	3.145	1.00	7.36
ATOM	40	CG	ASP A	6	-2.443	10.571	2.760	1.00	8.26
ATOM	41	OD1	ASP A	6	-1.756	9.679	3.294	1.00	8.11
30 ATOM	42	OD2	ASP A	6	-3.298	10.302	1.913	1.00	9.91
ATOM	43	C	ASP A	6	0.128	11.869	3.929	1.00	7.11
ATOM	44	O	ASP A	6	0.528	12.109	2.787	1.00	5.38
ATOM	45	N	TRP A	7	0.830	11.174	4.817	1.00	6.66
ATOM	46	CA	TRP A	7	2.207	10.800	4.561	1.00	5.18
35 ATOM	47	CB	TRP A	7	2.871	10.293	5.844	1.00	5.63
ATOM	48	CG	TRP A	7	3.106	11.375	6.857	1.00	3.75
ATOM	49	CD2	TRP A	7	4.099	12.415	6.796	1.00	5.24

ATOM	50	CE2	TRP	A	7	3.992	13.165	7.984	1.00	2.70
ATOM	51	CE3	TRP	A	7	5.075	12.776	5.852	1.00	4.91
ATOM	52	CD1	TRP	A	7	2.449	11.548	8.047	1.00	3.93
ATOM	53	NE1	TRP	A	7	2.978	12.618	8.725	1.00	2.42
5 ATOM	54	CZ2	TRP	A	7	4.823	14.250	8.260	1.00	3.41
ATOM	55	CZ3	TRP	A	7	5.899	13.855	6.131	1.00	3.27
ATOM	56	CH2	TRP	A	7	5.765	14.577	7.324	1.00	3.02
ATOM	57	C	TRP	A	7	2.384	9.826	3.415	1.00	6.34
ATOM	58	O	TRP	A	7	3.511	9.628	2.961	1.00	6.00
10 ATOM	59	N	ARG	A	8	1.288	9.221	2.939	1.00	7.07
ATOM	60	CA	ARG	A	8	1.360	8.301	1.801	1.00	7.88
ATOM	61	CB	ARG	A	8	0.018	7.613	1.510	1.00	6.47
ATOM	62	CG	ARG	A	8	-0.364	6.530	2.495	1.00	9.08
ATOM	63	CD	ARG	A	8	-1.711	5.920	2.164	1.00	9.74
15 ATOM	64	NE	ARG	A	8	-2.776	6.919	2.212	1.00	12.63
ATOM	65	CZ	ARG	A	8	-4.024	6.724	1.787	1.00	13.43
ATOM	66	NH1	ARG	A	8	-4.395	5.555	1.286	1.00	14.70
ATOM	67	NH2	ARG	A	8	-4.889	7.730	1.797	1.00	15.31
ATOM	68	C	ARG	A	8	1.767	9.093	0.577	1.00	9.94
20 ATOM	69	O	ARG	A	8	2.504	8.607	-0.276	1.00	10.87
ATOM	70	N	GLU	A	9	1.318	10.337	0.505	1.00	11.77
ATOM	71	CA	GLU	A	9	1.640	11.189	-0.637	1.00	14.34
ATOM	72	CB	GLU	A	9	0.759	12.442	-0.616	1.00	16.42
ATOM	73	CG	GLU	A	9	-0.728	12.126	-0.802	1.00	19.57
25 ATOM	74	CD	GLU	A	9	-1.647	13.323	-0.558	1.00	21.78
ATOM	75	OE1	GLU	A	9	-1.218	14.309	0.096	1.00	22.24
ATOM	76	OE2	GLU	A	9	-2.817	13.266	-1.008	1.00	23.66
ATOM	77	C	GLU	A	9	3.116	11.576	-0.706	1.00	13.25
ATOM	78	O	GLU	A	9	3.571	12.112	-1.719	1.00	15.61
30 ATOM	79	N	LYS	A	10	3.867	11.282	0.351	1.00	11.63
ATOM	80	CA	LYS	A	10	5.284	11.613	0.393	1.00	11.92
ATOM	81	CB	LYS	A	10	5.572	12.522	1.592	1.00	10.96
ATOM	82	CG	LYS	A	10	4.880	13.872	1.461	1.00	11.07
ATOM	83	CD	LYS	A	10	5.408	14.884	2.421	1.00	9.57
35 ATOM	84	CE	LYS	A	10	4.714	16.219	2.224	1.00	10.48
ATOM	85	NZ	LYS	A	10	5.081	17.093	3.357	1.00	12.29
ATOM	86	C	LYS	A	10	6.274	10.450	0.334	1.00	11.29

ATOM	87	O	LYS	A	10	7.466	10.662	0.499	1.00	13.17
ATOM	88	N	GLY	A	11	5.787	9.231	0.098	1.00	12.10
ATOM	89	CA	GLY	A	11	6.663	8.062	0.011	1.00	8.89
ATOM	90	C	GLY	A	11	7.111	7.421	1.321	1.00	8.67
5 ATOM	91	O	GLY	A	11	8.036	6.614	1.319	1.00	8.22
ATOM	92	N	TYR	A	12	6.425	7.753	2.417	1.00	5.70
ATOM	93	CA	TYR	A	12	6.714	7.270	3.772	1.00	4.43
ATOM	94	CB	TYR	A	12	6.166	8.304	4.755	1.00	5.23
ATOM	95	CG	TYR	A	12	7.068	9.466	5.081	1.00	4.74
10 ATOM	96	CD1	TYR	A	12	7.405	10.416	4.120	1.00	5.67
ATOM	97	CE1	TYR	A	12	8.183	11.526	4.449	1.00	6.04
ATOM	98	CD2	TYR	A	12	7.528	9.645	6.375	1.00	6.11
ATOM	99	CE2	TYR	A	12	8.300	10.740	6.720	1.00	8.08
ATOM	100	CZ	TYR	A	12	8.621	11.680	5.752	1.00	8.16
15 ATOM	101	OH	TYR	A	12	9.355	12.783	6.123	1.00	11.13
ATOM	102	C	TYR	A	12	6.099	5.913	4.209	1.00	4.43
ATOM	103	O	TYR	A	12	6.466	5.367	5.271	1.00	2.69
ATOM	104	N	VAL	A	13	5.144	5.407	3.426	1.00	2.65
ATOM	105	CA	VAL	A	13	4.400	4.194	3.783	1.00	3.43
20 ATOM	106	CB	VAL	A	13	2.902	4.563	4.072	1.00	3.74
ATOM	107	CG1	VAL	A	13	2.185	3.449	4.832	1.00	5.21
ATOM	108	CG2	VAL	A	13	2.806	5.871	4.843	1.00	2.23
ATOM	109	C	VAL	A	13	4.422	3.037	2.785	1.00	2.70
ATOM	110	O	VAL	A	13	4.258	3.216	1.568	1.00	2.00
25 ATOM	111	N	THR	A	14	4.611	1.834	3.309	1.00	3.78
ATOM	112	CA	THR	A	14	4.607	0.648	2.471	1.00	2.88
ATOM	113	CB	THR	A	14	5.360	-0.520	3.119	1.00	2.00
ATOM	114	OG1	THR	A	14	4.865	-0.733	4.443	1.00	2.99
ATOM	115	CG2	THR	A	14	6.855	-0.273	3.110	1.00	2.00
30 ATOM	116	C	THR	A	14	3.164	0.203	2.284	1.00	2.85
ATOM	117	O	THR	A	14	2.263	0.623	3.016	1.00	4.31
ATOM	118	N	PRO	A	15	2.926	-0.647	1.287	1.00	3.14
ATOM	119	CD	PRO	A	15	3.863	-1.097	0.237	1.00	3.37
ATOM	120	CA	PRO	A	15	1.572	-1.141	1.035	1.00	3.31
35 ATOM	121	CB	PRO	A	15	1.796	-2.151	-0.082	1.00	3.57
ATOM	122	CG	PRO	A	15	2.930	-1.516	-0.862	1.00	2.31
ATOM	123	C	PRO	A	15	1.001	-1.804	2.278	1.00	4.50

	ATOM	124	O	PRO	A	15	1.730	-2.147	3.225	1.00	7.69
	ATOM	125	N	VAL	A	16	-0.312	-1.932	2.314	1.00	3.95
	ATOM	126	CA	VAL	A	16	-0.951	-2.561	3.439	1.00	4.19
	ATOM	127	CB	VAL	A	16	-2.460	-2.467	3.285	1.00	4.60
5	ATOM	128	CG1	VAL	A	16	-3.181	-3.317	4.329	1.00	5.37
	ATOM	129	CG2	VAL	A	16	-2.865	-1.019	3.440	1.00	5.35
	ATOM	130	C	VAL	A	16	-0.476	-4.018	3.538	1.00	4.85
	ATOM	131	O	VAL	A	16	-0.230	-4.661	2.521	1.00	2.91
	ATOM	132	N	LYS	A	17	-0.246	-4.480	4.768	1.00	5.25
10	ATOM	133	CA	LYS	A	17	0.186	-5.859	5.035	1.00	5.74
	ATOM	134	CB	LYS	A	17	1.448	-5.867	5.891	1.00	6.60
	ATOM	135	CG	LYS	A	17	2.670	-5.316	5.171	1.00	5.83
	ATOM	136	CD	LYS	A	17	3.769	-5.064	6.139	1.00	5.40
	ATOM	137	CE	LYS	A	17	4.928	-4.378	5.459	1.00	7.08
15	ATOM	138	NZ	LYS	A	17	5.991	-4.112	6.466	1.00	4.70
	ATOM	139	C	LYS	A	17	-0.932	-6.634	5.742	1.00	6.36
	ATOM	140	O	LYS	A	17	-2.000	-6.090	5.995	1.00	6.25
	ATOM	141	N	ASN	A	18	-0.699	-7.904	6.053	1.00	7.06
	ATOM	142	CA	ASN	A	18	-1.724	-8.717	6.715	1.00	8.00
20	ATOM	143	CB	ASN	A	18	-2.471	-9.555	5.675	1.00	9.18
	ATOM	144	CG	ASN	A	18	-3.767	-10.120	6.210	1.00	9.76
	ATOM	145	OD1	ASN	A	18	-3.947	-10.239	7.430	1.00	11.21
	ATOM	146	ND2	ASN	A	18	-4.701	-10.440	5.303	1.00	10.47
	ATOM	147	C	ASN	A	18	-1.095	-9.612	7.792	1.00	7.45
25	ATOM	148	O	ASN	A	18	-0.224	-10.433	7.515	1.00	9.35
	ATOM	149	N	GLN	A	19	-1.530	-9.436	9.024	1.00	7.64
	ATOM	150	CA	GLN	A	19	-0.975	-10.187	10.143	1.00	8.88
	ATOM	151	CB	GLN	A	19	-1.239	-9.438	11.458	1.00	6.97
	ATOM	152	CG	GLN	A	19	-2.703	-9.348	11.796	1.00	8.46
30	ATOM	153	CD	GLN	A	19	-2.995	-8.525	13.021	1.00	8.38
	ATOM	154	OE1	GLN	A	19	-3.096	-7.307	12.951	1.00	11.05
	ATOM	155	NE2	GLN	A	19	-3.197	-9.190	14.147	1.00	9.98
	ATOM	156	C	GLN	A	19	-1.501	-11.629	10.243	1.00	10.55
	ATOM	157	O	GLN	A	19	-0.978	-12.426	11.023	1.00	10.56
35	ATOM	158	N	GLY	A	20	-2.528	-11.951	9.461	1.00	11.52
	ATOM	159	CA	GLY	A	20	-3.120	-13.282	9.505	1.00	14.78
	ATOM	160	C	GLY	A	20	-3.689	-13.642	10.876	1.00	16.31

ATOM	161	O	GLY A	20	-4.133	-12.778	11.634	1.00	14.92
ATOM	162	N	GLN A	21	-3.663	-14.933	11.191	1.00	18.50
ATOM	163	CA	GLN A	21	-4.146	-15.474	12.463	1.00	21.24
ATOM	164	CB	GLN A	21	-4.640	-16.915	12.248	1.00	24.70
5 ATOM	165	CG	GLN A	21	-6.094	-17.040	11.789	1.00	28.58
ATOM	166	CD	GLN A	21	-7.086	-16.847	12.936	1.00	31.08
ATOM	167	OE1	GLN A	21	-6.907	-17.390	14.034	1.00	32.46
ATOM	168	NE2	GLN A	21	-8.141	-16.070	12.683	1.00	31.53
ATOM	169	C	GLN A	21	-3.033	-15.448	13.519	1.00	19.56
10 ATOM	170	O	GLN A	21	-2.633	-16.485	14.067	1.00	21.26
ATOM	171	N	CYS A	22	-2.503	-14.259	13.764	1.00	15.59
ATOM	172	CA	CYS A	22	-1.433	-14.074	14.730	1.00	11.69
ATOM	173	C	CYS A	22	-1.636	-12.682	15.350	1.00	11.27
ATOM	174	O	CYS A	22	-1.967	-11.724	14.643	1.00	10.21
15 ATOM	175	CB	CYS A	22	-0.082	-14.196	14.011	1.00	10.01
ATOM	176	SG	CYS A	22	1.384	-13.661	14.947	1.00	9.82
ATOM	177	N	GLY A	23	-1.569	-12.599	16.675	1.00	10.96
ATOM	178	CA	GLY A	23	-1.750	-11.327	17.359	1.00	9.90
ATOM	179	C	GLY A	23	-0.460	-10.528	17.340	1.00	7.69
20 ATOM	180	O	GLY A	23	0.146	-10.290	18.382	1.00	5.44
ATOM	181	N	SER A	24	-0.066	-10.111	16.139	1.00	6.31
ATOM	182	CA	SER A	24	1.172	-9.369	15.916	1.00	6.11
ATOM	183	CB	SER A	24	2.017	-10.147	14.919	1.00	3.13
ATOM	184	OG	SER A	24	1.220	-10.487	13.804	1.00	2.22
25 ATOM	185	C	SER A	24	0.952	-7.939	15.390	1.00	5.17
ATOM	186	O	SER A	24	1.857	-7.348	14.817	1.00	4.46
ATOM	187	N	CYS A	25	-0.244	-7.395	15.602	1.00	6.02
ATOM	188	CA	CYS A	25	-0.576	-6.041	15.148	1.00	8.54
ATOM	189	CB	CYS A	25	-1.987	-5.644	15.612	1.00	10.76
30 ATOM	190	SG	CYS A	25	-2.253	-5.670	17.388	1.00	16.00
ATOM	191	C	CYS A	25	0.451	-5.046	15.678	1.00	7.98
ATOM	192	O	CYS A	25	0.840	-4.093	14.995	1.00	6.80
ATOM	193	N	TRP A	26	0.912	-5.306	16.900	1.00	6.81
ATOM	194	CA	TRP A	26	1.910	-4.475	17.542	1.00	5.51
35 ATOM	195	CB	TRP A	26	2.227	-5.017	18.942	1.00	5.06
ATOM	196	CG	TRP A	26	2.707	-6.451	18.963	1.00	5.62
ATOM	197	CD2	TRP A	26	4.071	-6.907	18.857	1.00	4.05

ATOM	198	CE2	TRP	A	26	4.044	-8.320	18.906	1.00	3.12
ATOM	199	CE3	TRP	A	26	5.308	-6.256	18.721	1.00	2.00
ATOM	200	CD1	TRP	A	26	1.933	-7.579	19.068	1.00	4.02
ATOM	201	NE1	TRP	A	26	2.732	-8.697	19.031	1.00	5.11
5 ATOM	202	CZ2	TRP	A	26	5.210	-9.102	18.829	1.00	3.13
ATOM	203	CZ3	TRP	A	26	6.474	-7.044	18.639	1.00	2.32
ATOM	204	CH2	TRP	A	26	6.408	-8.449	18.696	1.00	2.00
ATOM	205	C	TRP	A	26	3.177	-4.415	16.679	1.00	5.29
ATOM	206	O	TRP	A	26	3.841	-3.384	16.625	1.00	3.85
10 ATOM	207	N	ALA	A	27	3.483	-5.514	15.990	1.00	3.57
ATOM	208	CA	ALA	A	27	4.661	-5.594	15.130	1.00	3.43
ATOM	209	CB	ALA	A	27	5.094	-7.082	14.916	1.00	2.00
ATOM	210	C	ALA	A	27	4.469	-4.865	13.802	1.00	2.20
ATOM	211	O	ALA	A	27	5.410	-4.267	13.305	1.00	3.00
15 ATOM	212	N	PHE	A	28	3.262	-4.908	13.229	1.00	2.67
ATOM	213	CA	PHE	A	28	2.983	-4.215	11.968	1.00	3.09
ATOM	214	CB	PHE	A	28	1.677	-4.714	11.320	1.00	2.99
ATOM	215	CG	PHE	A	28	1.801	-6.090	10.688	1.00	2.39
ATOM	216	CD1	PHE	A	28	1.810	-7.236	11.483	1.00	2.92
20 ATOM	217	CD2	PHE	A	28	2.011	-6.227	9.318	1.00	2.00
ATOM	218	CE1	PHE	A	28	2.036	-8.494	10.919	1.00	2.00
ATOM	219	CE2	PHE	A	28	2.240	-7.473	8.753	1.00	2.00
ATOM	220	CZ	PHE	A	28	2.255	-8.604	9.550	1.00	2.00
ATOM	221	C	PHE	A	28	2.914	-2.705	12.217	1.00	3.35
25 ATOM	222	O	PHE	A	28	3.281	-1.903	11.355	1.00	5.15
ATOM	223	N	SER	A	29	2.451	-2.321	13.402	1.00	2.49
ATOM	224	CA	SER	A	29	2.366	-0.909	13.760	1.00	2.00
ATOM	225	CB	SER	A	29	1.524	-0.746	15.010	1.00	2.00
ATOM	226	OG	SER	A	29	1.394	0.609	15.394	1.00	2.70
30 ATOM	227	C	SER	A	29	3.779	-0.368	13.980	1.00	2.00
ATOM	228	O	SER	A	29	4.114	0.720	13.505	1.00	4.83
ATOM	229	N	ALA	A	30	4.619	-1.159	14.644	1.00	2.00
ATOM	230	CA	ALA	A	30	5.993	-0.778	14.926	1.00	2.14
ATOM	231	CB	ALA	A	30	6.634	-1.761	15.921	1.00	2.00
35 ATOM	232	C	ALA	A	30	6.838	-0.650	13.664	1.00	2.00
ATOM	233	O	ALA	A	30	7.583	0.318	13.521	1.00	4.26
ATOM	234	N	THR	A	31	6.731	-1.613	12.744	1.00	4.13

	ATOM	235	CA	THR	A	31	7.486	-1.551	11.490	1.00	2.32
	ATOM	236	CB	THR	A	31	7.417	-2.870	10.668	1.00	2.61
	ATOM	237	OG1	THR	A	31	6.048	-3.226	10.450	1.00	4.22
	ATOM	238	CG2	THR	A	31	8.186	-4.038	11.357	1.00	2.00
5	ATOM	239	C	THR	A	31	6.923	-0.398	10.632	1.00	2.96
	ATOM	240	O	THR	A	31	7.660	0.233	9.869	1.00	2.64
	ATOM	241	N	GLY	A	32	5.615	-0.158	10.721	1.00	2.07
	ATOM	242	CA	GLY	A	32	5.019	0.935	9.970	1.00	2.00
	ATOM	243	C	GLY	A	32	5.638	2.259	10.379	1.00	2.00
10	ATOM	244	O	GLY	A	32	6.079	3.045	9.545	1.00	2.21
	ATOM	245	N	ALA	A	33	5.686	2.493	11.683	1.00	2.47
	ATOM	246	CA	ALA	A	33	6.286	3.694	12.260	1.00	2.46
	ATOM	247	CB	ALA	A	33	6.055	3.706	13.762	1.00	2.00
	ATOM	248	C	ALA	A	33	7.796	3.765	11.946	1.00	3.23
15	ATOM	249	O	ALA	A	33	8.282	4.826	11.585	1.00	2.50
	ATOM	250	N	LEU	A	34	8.533	2.656	12.079	1.00	2.77
	ATOM	251	CA	LEU	A	34	9.977	2.663	11.780	1.00	2.95
	ATOM	252	CB	LEU	A	34	10.684	1.397	12.304	1.00	4.24
	ATOM	253	CG	LEU	A	34	12.215	1.295	12.145	1.00	3.68
20	ATOM	254	CD1	LEU	A	34	12.954	2.581	12.640	1.00	2.00
	ATOM	255	CD2	LEU	A	34	12.694	0.085	12.936	1.00	2.56
	ATOM	256	C	LEU	A	34	10.263	2.861	10.296	1.00	2.58
	ATOM	257	O	LEU	A	34	11.244	3.489	9.931	1.00	3.87
	ATOM	258	N	GLU	A	35	9.392	2.340	9.442	1.00	2.37
25	ATOM	259	CA	GLU	A	35	9.549	2.496	8.001	1.00	3.81
	ATOM	260	CB	GLU	A	35	8.467	1.700	7.251	1.00	4.26
	ATOM	261	CG	GLU	A	35	8.723	0.181	7.159	1.00	4.41
	ATOM	262	CD	GLU	A	35	7.475	-0.626	6.916	1.00	6.77
	ATOM	263	OE1	GLU	A	35	6.373	-0.047	6.741	1.00	6.95
30	ATOM	264	OE2	GLU	A	35	7.587	-1.865	6.896	1.00	7.64
	ATOM	265	C	GLU	A	35	9.471	3.987	7.632	1.00	4.62
	ATOM	266	O	GLU	A	35	10.244	4.462	6.788	1.00	4.48
	ATOM	267	N	GLY	A	36	8.575	4.715	8.300	1.00	2.53
	ATOM	268	CA	GLY	A	36	8.419	6.137	8.061	1.00	2.91
35	ATOM	269	C	GLY	A	36	9.614	6.927	8.559	1.00	4.17
	ATOM	270	O	GLY	A	36	10.101	7.824	7.866	1.00	6.97
	ATOM	271	N	GLN	A	37	10.107	6.594	9.748	1.00	3.54

	ATOM	272	CA	GLN A	37	11.248	7.302	10.285	1.00	3.67
	ATOM	273	CB	GLN A	37	11.409	7.065	11.776	1.00	2.49
	ATOM	274	CG	GLN A	37	10.277	7.637	12.607	1.00	5.01
	ATOM	275	CD	GLN A	37	10.000	9.107	12.316	1.00	3.24
5	ATOM	276	OE1	GLN A	37	10.769	9.981	12.718	1.00	5.78
	ATOM	277	NE2	GLN A	37	8.915	9.380	11.617	1.00	2.02
	ATOM	278	C	GLN A	37	12.537	7.016	9.537	1.00	6.45
	ATOM	279	O	GLN A	37	13.387	7.898	9.434	1.00	7.80
	ATOM	280	N	MET A	38	12.701	5.797	9.029	1.00	5.74
10	ATOM	281	CA	MET A	38	13.896	5.460	8.257	1.00	7.86
	ATOM	282	CB	MET A	38	14.007	3.953	7.964	1.00	7.31
	ATOM	283	CG	MET A	38	14.406	3.093	9.147	1.00	6.19
	ATOM	284	SD	MET A	38	15.946	3.583	9.892	1.00	6.69
	ATOM	285	CE	MET A	38	16.960	3.664	8.429	1.00	2.57
15	ATOM	286	C	MET A	38	13.837	6.233	6.948	1.00	9.64
	ATOM	287	O	MET A	38	14.869	6.661	6.420	1.00	9.28
	ATOM	288	N	PHE A	39	12.626	6.394	6.412	1.00	10.04
	ATOM	289	CA	PHE A	39	12.454	7.148	5.193	1.00	9.68
	ATOM	290	CB	PHE A	39	11.047	6.979	4.613	1.00	10.54
20	ATOM	291	CG	PHE A	39	10.854	7.685	3.299	1.00	11.39
	ATOM	292	CD1	PHE A	39	11.103	7.027	2.094	1.00	11.41
	ATOM	293	CD2	PHE A	39	10.460	9.019	3.263	1.00	12.49
	ATOM	294	CE1	PHE A	39	10.970	7.676	0.881	1.00	11.60
	ATOM	295	CE2	PHE A	39	10.321	9.689	2.049	1.00	12.07
25	ATOM	296	CZ	PHE A	39	10.577	9.017	0.855	1.00	13.19
	ATOM	297	C	PHE A	39	12.754	8.623	5.468	1.00	9.58
	ATOM	298	O	PHE A	39	13.438	9.255	4.686	1.00	12.10
	ATOM	299	N	ARG A	40	12.262	9.158	6.581	1.00	11.25
	ATOM	300	CA	ARG A	40	12.504	10.555	6.956	1.00	12.04
30	ATOM	301	CB	ARG A	40	11.844	10.847	8.304	1.00	11.50
	ATOM	302	CG	ARG A	40	12.173	12.195	8.950	1.00	11.61
	ATOM	303	CD	ARG A	40	11.646	12.213	10.373	1.00	14.39
	ATOM	304	NE	ARG A	40	11.588	13.549	10.969	1.00	15.72
	ATOM	305	CZ	ARG A	40	11.643	13.800	12.278	1.00	16.09
35	ATOM	306	NH1	ARG A	40	11.760	12.811	13.152	1.00	15.42
	ATOM	307	NH2	ARG A	40	11.558	15.050	12.723	1.00	15.62
	ATOM	308	C	ARG A	40	14.013	10.825	7.051	1.00	13.28

ATOM	309	O	ARG A	40	14.485	11.912	6.723	1.00	13.32
ATOM	310	N	LYS A	41	14.766	9.819	7.485	1.00	14.01
ATOM	311	CA	LYS A	41	16.211	9.929	7.624	1.00	13.57
ATOM	312	CB	LYS A	41	16.692	8.939	8.677	1.00	13.59
5 ATOM	313	CG	LYS A	41	18.199	8.909	8.844	1.00	14.72
ATOM	314	CD	LYS A	41	18.644	7.794	9.782	1.00	16.77
ATOM	315	CE	LYS A	41	20.126	7.831	10.058	1.00	18.29
ATOM	316	NZ	LYS A	41	20.924	7.748	8.795	1.00	21.26
ATOM	317	C	LYS A	41	17.029	9.725	6.339	1.00	14.01
10 ATOM	318	O	LYS A	41	17.961	10.485	6.072	1.00	15.48
ATOM	319	N	THR A	42	16.676	8.717	5.542	1.00	12.25
ATOM	320	CA	THR A	42	17.427	8.378	4.331	1.00	10.80
ATOM	321	CB	THR A	42	17.848	6.887	4.351	1.00	10.53
ATOM	322	OG1	THR A	42	16.703	6.061	4.060	1.00	9.82
15 ATOM	323	CG2	THR A	42	18.411	6.510	5.717	1.00	6.89
ATOM	324	C	THR A	42	16.751	8.590	2.989	1.00	11.11
ATOM	325	O	THR A	42	17.405	8.534	1.949	1.00	12.23
ATOM	326	N	GLY A	43	15.437	8.745	2.988	1.00	11.19
ATOM	327	CA	GLY A	43	14.737	8.918	1.728	1.00	12.38
20 ATOM	328	C	GLY A	43	14.509	7.612	0.977	1.00	12.46
ATOM	329	O	GLY A	43	14.161	7.630	-0.207	1.00	12.41
ATOM	330	N	ALA A	44	14.698	6.480	1.657	1.00	12.34
ATOM	331	CA	ALA A	44	14.491	5.168	1.039	1.00	11.41
ATOM	332	CB	ALA A	44	15.806	4.366	1.004	1.00	11.51
25 ATOM	333	C	ALA A	44	13.428	4.419	1.830	1.00	10.15
ATOM	334	O	ALA A	44	13.487	4.369	3.063	1.00	10.10
ATOM	335	N	LEU A	45	12.422	3.904	1.128	1.00	8.85
ATOM	336	CA	LEU A	45	11.339	3.150	1.763	1.00	7.67
ATOM	337	CB	LEU A	45	9.985	3.444	1.096	1.00	4.50
30 ATOM	338	CG	LEU A	45	8.769	2.740	1.723	1.00	4.04
ATOM	339	CD1	LEU A	45	8.539	3.204	3.165	1.00	2.51
ATOM	340	CD2	LEU A	45	7.518	2.974	0.883	1.00	3.79
ATOM	341	C	LEU A	45	11.627	1.665	1.669	1.00	6.73
ATOM	342	O	LEU A	45	11.572	1.096	0.592	1.00	7.76
35 ATOM	343	N	ILE A	46	11.974	1.044	2.796	1.00	8.21
ATOM	344	CA	ILE A	46	12.255	-0.395	2.817	1.00	7.41
ATOM	345	CB	ILE A	46	13.728	-0.700	3.237	1.00	7.58

ATOM	346	CG2	ILE	A	46	14.013	-2.222	3.131	1.00	8.78
ATOM	347	CG1	ILE	A	46	14.715	0.089	2.367	1.00	9.49
ATOM	348	CD1	ILE	A	46	16.173	-0.074	2.783	1.00	10.00
ATOM	349	C	ILE	A	46	11.301	-1.116	3.783	1.00	6.16
5 ATOM	350	O	ILE	A	46	11.241	-0.786	4.968	1.00	6.62
ATOM	351	N	SER	A	47	10.546	-2.085	3.273	1.00	5.59
ATOM	352	CA	SER	A	47	9.630	-2.847	4.114	1.00	6.27
ATOM	353	CB	SER	A	47	8.764	-3.767	3.253	1.00	5.22
ATOM	354	OG	SER	A	47	7.738	-4.356	4.021	1.00	7.41
10 ATOM	355	C	SER	A	47	10.451	-3.636	5.157	1.00	5.90
ATOM	356	O	SER	A	47	11.492	-4.234	4.835	1.00	4.59
ATOM	357	N	LEU	A	48	10.019	-3.574	6.417	1.00	5.25
ATOM	358	CA	LEU	A	48	10.717	-4.226	7.529	1.00	5.28
ATOM	359	CB	LEU	A	48	10.895	-3.229	8.685	1.00	4.88
15 ATOM	360	CG	LEU	A	48	11.595	-1.897	8.317	1.00	5.79
ATOM	361	CD1	LEU	A	48	11.445	-0.883	9.440	1.00	3.48
ATOM	362	CD2	LEU	A	48	13.075	-2.129	8.009	1.00	4.77
ATOM	363	C	LEU	A	48	10.045	-5.506	8.022	1.00	5.07
ATOM	364	O	LEU	A	48	8.834	-5.682	7.906	1.00	4.73
20 ATOM	365	N	SER	A	49	10.836	-6.355	8.660	1.00	5.94
ATOM	366	CA	SER	A	49	10.382	-7.651	9.155	1.00	4.45
ATOM	367	CB	SER	A	49	11.588	-8.592	9.250	1.00	6.13
ATOM	368	OG	SER	A	49	11.220	-9.886	9.690	1.00	8.26
ATOM	369	C	SER	A	49	9.580	-7.714	10.448	1.00	2.44
25 ATOM	370	O	SER	A	49	10.111	-7.541	11.551	1.00	2.00
ATOM	371	N	GLU	A	50	8.283	-7.959	10.313	1.00	2.00
ATOM	372	CA	GLU	A	50	7.446	-8.114	11.489	1.00	3.02
ATOM	373	CB	GLU	A	50	5.962	-8.130	11.120	1.00	4.09
ATOM	374	CG	GLU	A	50	5.408	-6.788	10.663	1.00	2.50
30 ATOM	375	CD	GLU	A	50	5.660	-6.518	9.199	1.00	5.11
ATOM	376	OE1	GLU	A	50	5.945	-7.463	8.448	1.00	7.22
ATOM	377	OE2	GLU	A	50	5.553	-5.360	8.774	1.00	7.90
ATOM	378	C	GLU	A	50	7.815	-9.451	12.126	1.00	2.00
ATOM	379	O	GLU	A	50	7.712	-9.606	13.322	1.00	3.82
35 ATOM	380	N	GLN	A	51	8.251	-10.410	11.313	1.00	4.25
ATOM	381	CA	GLN	A	51	8.622	-11.731	11.818	1.00	3.90
ATOM	382	CB	GLN	A	51	8.869	-12.704	10.668	1.00	2.10

	ATOM	383	CG	GLN	A	51	8.780	-14.206	11.068	1.00	2.85
	ATOM	384	CD	GLN	A	51	7.434	-14.576	11.684	1.00	2.00
	ATOM	385	OE1	GLN	A	51	6.389	-14.312	11.112	1.00	2.00
	ATOM	386	NE2	GLN	A	51	7.464	-15.193	12.852	1.00	2.68
5	ATOM	387	C	GLN	A	51	9.845	-11.628	12.735	1.00	3.62
	ATOM	388	O	GLN	A	51	9.873	-12.277	13.788	1.00	2.53
	ATOM	389	N	ASP	A	52	10.794	-10.747	12.373	1.00	3.63
	ATOM	390	CA	ASP	A	52	11.994	-10.491	13.161	1.00	2.57
	ATOM	391	CB	ASP	A	52	12.835	-9.375	12.517	1.00	3.71
10	ATOM	392	CG	ASP	A	52	14.259	-9.262	13.098	1.00	2.59
	ATOM	393	OD1	ASP	A	52	14.531	-9.695	14.234	1.00	3.36
	ATOM	394	OD2	ASP	A	52	15.128	-8.711	12.399	1.00	2.44
	ATOM	395	C	ASP	A	52	11.565	-10.083	14.567	1.00	4.37
	ATOM	396	O	ASP	A	52	12.081	-10.608	15.563	1.00	3.75
15	ATOM	397	N	LEU	A	53	10.607	-9.158	14.641	1.00	2.86
	ATOM	398	CA	LEU	A	53	10.072	-8.675	15.915	1.00	2.00
	ATOM	399	CB	LEU	A	53	9.085	-7.532	15.658	1.00	2.60
	ATOM	400	CG	LEU	A	53	9.652	-6.204	15.164	1.00	2.67
	ATOM	401	CD1	LEU	A	53	8.493	-5.237	14.963	1.00	2.00
20	ATOM	402	CD2	LEU	A	53	10.675	-5.655	16.189	1.00	2.00
	ATOM	403	C	LEU	A	53	9.361	-9.768	16.729	1.00	2.00
	ATOM	404	O	LEU	A	53	9.631	-9.943	17.931	1.00	2.00
	ATOM	405	N	VAL	A	54	8.421	-10.458	16.073	1.00	3.82
	ATOM	406	CA	VAL	A	54	7.619	-11.533	16.681	1.00	4.97
25	ATOM	407	CB	VAL	A	54	6.610	-12.172	15.592	1.00	4.86
	ATOM	408	CG1	VAL	A	54	5.887	-13.410	16.124	1.00	3.66
	ATOM	409	CG2	VAL	A	54	5.543	-11.155	15.186	1.00	4.34
	ATOM	410	C	VAL	A	54	8.519	-12.603	17.342	1.00	4.50
	ATOM	411	O	VAL	A	54	8.348	-12.928	18.509	1.00	5.80
30	ATOM	412	N	ASP	A	55	9.545	-13.040	16.616	1.00	6.09
	ATOM	413	CA	ASP	A	55	10.476	-14.079	17.064	1.00	4.92
	ATOM	414	CB	ASP	A	55	11.230	-14.674	15.860	1.00	3.20
	ATOM	415	CG	ASP	A	55	10.337	-15.304	14.818	1.00	3.85
	ATOM	416	OD1	ASP	A	55	9.150	-15.595	15.091	1.00	4.72
35	ATOM	417	OD2	ASP	A	55	10.857	-15.536	13.703	1.00	2.72
	ATOM	418	C	ASP	A	55	11.580	-13.641	18.014	1.00	6.95
	ATOM	419	O	ASP	A	55	12.158	-14.469	18.720	1.00	7.17

	ATOM	420	N	CYS A	56	11.952	-12.366	17.975	1.00	8.58
	ATOM	421	CA	CYS A	56	13.084	-11.938	18.776	1.00	6.99
	ATOM	422	C	CYS A	56	12.895	-10.988	19.927	1.00	7.01
	ATOM	423	O	CYS A	56	13.787	-10.883	20.769	1.00	10.34
5	ATOM	424	CB	CYS A	56	14.137	-11.350	17.847	1.00	5.98
	ATOM	425	SG	CYS A	56	14.501	-12.313	16.357	1.00	6.00
	ATOM	426	N	SER A	57	11.779	-10.278	19.987	1.00	9.08
	ATOM	427	CA	SER A	57	11.612	-9.303	21.068	1.00	10.69
	ATOM	428	CB	SER A	57	10.918	-8.034	20.568	1.00	8.58
10	ATOM	429	OG	SER A	57	9.566	-8.285	20.294	1.00	9.77
	ATOM	430	C	SER A	57	10.988	-9.781	22.372	1.00	11.68
	ATOM	431	O	SER A	57	10.432	-8.993	23.134	1.00	12.62
	ATOM	432	N	GLY A	58	11.121	-11.071	22.651	1.00	13.83
	ATOM	433	CA	GLY A	58	10.610	-11.608	23.895	1.00	11.63
15	ATOM	434	C	GLY A	58	11.292	-10.972	25.093	1.00	11.54
	ATOM	435	O	GLY A	58	10.626	-10.642	26.071	1.00	11.23
	ATOM	436	N	PRO A	59	12.611	-10.727	25.041	1.00	12.29
	ATOM	437	CD	PRO A	59	13.594	-11.044	23.993	1.00	11.81
	ATOM	438	CA	PRO A	59	13.272	-10.115	26.199	1.00	11.93
20	ATOM	439	CB	PRO A	59	14.719	-9.992	25.728	1.00	13.40
	ATOM	440	CG	PRO A	59	14.869	-11.106	24.763	1.00	12.49
	ATOM	441	C	PRO A	59	12.702	-8.735	26.584	1.00	12.46
	ATOM	442	O	PRO A	59	12.724	-8.346	27.758	1.00	12.90
	ATOM	443	N	GLN A	60	12.163	-8.020	25.601	1.00	10.55
25	ATOM	444	CA	GLN A	60	11.605	-6.691	25.830	1.00	8.86
	ATOM	445	CB	GLN A	60	11.714	-5.849	24.540	1.00	7.26
	ATOM	446	CG	GLN A	60	13.155	-5.391	24.210	1.00	6.32
	ATOM	447	CD	GLN A	60	14.102	-6.498	23.724	1.00	6.43
	ATOM	448	OE1	GLN A	60	15.333	-6.364	23.797	1.00	7.70
30	ATOM	449	NE2	GLN A	60	13.543	-7.546	23.158	1.00	3.38
	ATOM	450	C	GLN A	60	10.183	-6.676	26.410	1.00	7.36
	ATOM	451	O	GLN A	60	9.701	-5.630	26.821	1.00	6.68
	ATOM	452	N	GLY A	61	9.544	-7.844	26.483	1.00	5.53
	ATOM	453	CA	GLY A	61	8.209	-7.933	27.032	1.00	5.09
35	ATOM	454	C	GLY A	61	7.161	-8.339	26.015	1.00	7.10
	ATOM	455	O	GLY A	61	5.963	-8.385	26.320	1.00	9.01
	ATOM	456	N	ASN A	62	7.588	-8.551	24.776	1.00	7.60

ATOM	457	CA	ASN A	62	6.654	-8.953	23.725	1.00	9.01
ATOM	458	CB	ASN A	62	7.146	-8.537	22.331	1.00	6.76
ATOM	459	CG	ASN A	62	7.023	-7.033	22.092	1.00	6.05
ATOM	460	OD1	ASN A	62	7.785	-6.436	21.334	1.00	5.37
5 ATOM	461	ND2	ASN A	62	6.059	-6.421	22.741	1.00	3.19
ATOM	462	C	ASN A	62	6.431	-10.447	23.807	1.00	9.14
ATOM	463	O	ASN A	62	7.328	-11.196	24.198	1.00	9.09
ATOM	464	N	GLU A	63	5.213	-10.867	23.500	1.00	10.86
ATOM	465	CA	GLU A	63	4.867	-12.273	23.555	1.00	11.00
10 ATOM	466	CB	GLU A	63	3.867	-12.509	24.679	1.00	11.80
ATOM	467	CG	GLU A	63	4.503	-12.259	26.052	1.00	13.06
ATOM	468	CD	GLU A	63	3.661	-12.738	27.209	1.00	14.45
ATOM	469	OE1	GLU A	63	2.832	-13.650	27.026	1.00	18.29
ATOM	470	OE2	GLU A	63	3.826	-12.193	28.313	1.00	15.14
15 ATOM	471	C	GLU A	63	4.423	-12.886	22.233	1.00	10.77
ATOM	472	O	GLU A	63	3.382	-13.546	22.147	1.00	11.14
ATOM	473	N	GLY A	64	5.250	-12.678	21.211	1.00	10.35
ATOM	474	CA	GLY A	64	4.993	-13.223	19.887	1.00	10.93
ATOM	475	C	GLY A	64	3.616	-13.023	19.304	1.00	11.79
20 ATOM	476	O	GLY A	64	3.197	-11.888	19.077	1.00	11.98
ATOM	477	N	CYS A	65	2.907	-14.121	19.034	1.00	11.17
ATOM	478	CA	CYS A	65	1.571	-14.022	18.454	1.00	10.14
ATOM	479	C	CYS A	65	0.468	-13.822	19.469	1.00	10.16
ATOM	480	O	CYS A	65	-0.704	-13.808	19.110	1.00	11.53
25 ATOM	481	CB	CYS A	65	1.230	-15.234	17.572	1.00	9.54
ATOM	482	SG	CYS A	65	2.067	-15.291	15.961	1.00	10.24
ATOM	483	N	ASN A	66	0.823	-13.697	20.734	1.00	12.32
ATOM	484	CA	ASN A	66	-0.187	-13.482	21.764	1.00	14.74
ATOM	485	CB	ASN A	66	0.075	-14.386	22.956	1.00	15.93
30 ATOM	486	CG	ASN A	66	-0.198	-15.818	22.635	1.00	17.25
ATOM	487	OD1	ASN A	66	0.724	-16.637	22.569	1.00	19.52
ATOM	488	ND2	ASN A	66	-1.459	-16.129	22.362	1.00	15.97
ATOM	489	C	ASN A	66	-0.319	-12.032	22.218	1.00	14.67
ATOM	490	O	ASN A	66	-1.215	-11.700	23.016	1.00	15.81
35 ATOM	491	N	GLY A	67	0.563	-11.178	21.695	1.00	13.07
ATOM	492	CA	GLY A	67	0.530	-9.766	22.036	1.00	11.36
ATOM	493	C	GLY A	67	1.890	-9.134	22.235	1.00	8.74

	ATOM	494	O	GLY A	67	2.909	-9.825	22.326	1.00	8.51
	ATOM	495	N	GLY A	68	1.887	-7.807	22.328	1.00	7.52
	ATOM	496	CA	GLY A	68	3.105	-7.041	22.514	1.00	7.10
	ATOM	497	C	GLY A	68	2.805	-5.555	22.423	1.00	6.68
5	ATOM	498	O	GLY A	68	1.672	-5.177	22.161	1.00	7.62
	ATOM	499	N	LEU A	69	3.814	-4.718	22.640	1.00	7.01
	ATOM	500	CA	LEU A	69	3.659	-3.264	22.586	1.00	5.71
	ATOM	501	CB	LEU A	69	3.891	-2.631	23.955	1.00	7.16
	ATOM	502	CG	LEU A	69	3.055	-3.047	25.166	1.00	9.21
10	ATOM	503	CD1	LEU A	69	3.509	-2.219	26.375	1.00	10.10
	ATOM	504	CD2	LEU A	69	1.567	-2.864	24.906	1.00	8.93
	ATOM	505	C	LEU A	69	4.658	-2.678	21.607	1.00	5.71
	ATOM	506	O	LEU A	69	5.781	-3.147	21.491	1.00	4.13
	ATOM	507	N	MET A	70	4.237	-1.646	20.895	1.00	5.70
15	ATOM	508	CA	MET A	70	5.098	-0.982	19.926	1.00	5.04
	ATOM	509	CB	MET A	70	4.334	0.146	19.214	1.00	3.69
	ATOM	510	CG	MET A	70	3.213	-0.342	18.286	1.00	2.10
	ATOM	511	SD	MET A	70	1.712	-0.933	19.131	1.00	2.01
	ATOM	512	CE	MET A	70	0.824	0.573	19.277	1.00	2.00
20	ATOM	513	C	MET A	70	6.364	-0.452	20.569	1.00	3.03
	ATOM	514	O	MET A	70	7.440	-0.549	19.990	1.00	4.19
	ATOM	515	N	ASP A	71	6.249	0.064	21.787	1.00	3.16
	ATOM	516	CA	ASP A	71	7.422	0.575	22.479	1.00	2.25
	ATOM	517	CB	ASP A	71	7.029	1.307	23.740	1.00	2.00
25	ATOM	518	CG	ASP A	71	6.437	2.646	23.443	1.00	2.00
	ATOM	519	OD1	ASP A	71	6.532	3.094	22.281	1.00	2.00
	ATOM	520	OD2	ASP A	71	5.859	3.236	24.359	1.00	3.76
	ATOM	521	C	ASP A	71	8.416	-0.510	22.778	1.00	3.38
	ATOM	522	O	ASP A	71	9.615	-0.282	22.658	1.00	2.40
30	ATOM	523	N	TYR A	72	7.917	-1.698	23.115	1.00	2.72
	ATOM	524	CA	TYR A	72	8.790	-2.842	23.396	1.00	3.10
	ATOM	525	CB	TYR A	72	7.978	-4.052	23.878	1.00	3.23
	ATOM	526	CG	TYR A	72	7.390	-3.950	25.271	1.00	2.49
	ATOM	527	CD1	TYR A	72	7.770	-2.939	26.145	1.00	4.46
35	ATOM	528	CE1	TYR A	72	7.236	-2.859	27.418	1.00	4.52
	ATOM	529	CD2	TYR A	72	6.457	-4.884	25.714	1.00	2.65
	ATOM	530	CE2	TYR A	72	5.916	-4.818	26.983	1.00	3.69

ATOM	531	CZ	TYR	A	72	6.308	-3.807	27.821	1.00	5.94
ATOM	532	OH	TYR	A	72	5.749	-3.723	29.054	1.00	8.70
ATOM	533	C	TYR	A	72	9.550	-3.231	22.128	1.00	2.21
ATOM	534	O	TYR	A	72	10.666	-3.728	22.198	1.00	4.44
5 ATOM	535	N	ALA	A	73	8.925	-3.025	20.971	1.00	2.81
ATOM	536	CA	ALA	A	73	9.527	-3.328	19.680	1.00	2.00
ATOM	537	CB	ALA	A	73	8.456	-3.359	18.600	1.00	4.15
ATOM	538	C	ALA	A	73	10.597	-2.317	19.322	1.00	2.44
ATOM	539	O	ALA	A	73	11.615	-2.663	18.739	1.00	2.00
10 ATOM	540	N	PHE	A	74	10.332	-1.045	19.615	1.00	3.81
ATOM	541	CA	PHE	A	74	11.306	0.027	19.368	1.00	4.29
ATOM	542	CB	PHE	A	74	10.662	1.396	19.614	1.00	2.00
ATOM	543	CG	PHE	A	74	9.516	1.700	18.690	1.00	2.00
ATOM	544	CD1	PHE	A	74	8.407	2.407	19.150	1.00	2.28
15 ATOM	545	CD2	PHE	A	74	9.520	1.244	17.377	1.00	2.00
ATOM	546	CE1	PHE	A	74	7.315	2.650	18.317	1.00	2.00
ATOM	547	CE2	PHE	A	74	8.428	1.483	16.529	1.00	2.97
ATOM	548	CZ	PHE	A	74	7.325	2.189	17.012	1.00	2.00
ATOM	549	C	PHE	A	74	12.530	-0.200	20.285	1.00	2.69
20 ATOM	550	O	PHE	A	74	13.678	-0.007	19.873	1.00	4.23
ATOM	551	N	GLN	A	75	12.281	-0.631	21.521	1.00	3.82
ATOM	552	CA	GLN	A	75	13.365	-0.944	22.457	1.00	5.85
ATOM	553	CB	GLN	A	75	12.833	-1.253	23.854	1.00	8.10
ATOM	554	CG	GLN	A	75	13.956	-1.448	24.888	1.00	11.09
25 ATOM	555	CD	GLN	A	75	14.762	-0.182	25.129	1.00	12.81
ATOM	556	OE1	GLN	A	75	16.003	-0.168	25.067	1.00	12.82
ATOM	557	NE2	GLN	A	75	14.053	0.897	25.398	1.00	15.11
ATOM	558	C	GLN	A	75	14.216	-2.131	21.937	1.00	5.66
ATOM	559	O	GLN	A	75	15.437	-2.119	22.075	1.00	2.44
30 ATOM	560	N	TYR	A	76	13.568	-3.142	21.343	1.00	5.05
ATOM	561	CA	TYR	A	76	14.276	-4.299	20.751	1.00	4.41
ATOM	562	CB	TYR	A	76	13.281	-5.349	20.214	1.00	2.00
ATOM	563	CG	TYR	A	76	13.930	-6.360	19.274	1.00	2.07
ATOM	564	CD1	TYR	A	76	14.728	-7.387	19.768	1.00	2.47
35 ATOM	565	CE1	TYR	A	76	15.394	-8.253	18.912	1.00	2.00
ATOM	566	CD2	TYR	A	76	13.805	-6.230	17.892	1.00	2.00
ATOM	567	CE2	TYR	A	76	14.465	-7.085	17.022	1.00	2.22

	ATOM	568	CZ	TYR	A	76	15.264	-8.094	17.548	1.00	2.41
	ATOM	569	OH	TYR	A	76	15.977	-8.919	16.714	1.00	3.62
	ATOM	570	C	TYR	A	76	15.212	-3.884	19.605	1.00	4.56
	ATOM	571	O	TYR	A	76	16.347	-4.353	19.512	1.00	5.52
5	ATOM	572	N	VAL	A	77	14.702	-3.076	18.683	1.00	4.67
	ATOM	573	CA	VAL	A	77	15.498	-2.625	17.565	1.00	4.35
	ATOM	574	CB	VAL	A	77	14.697	-1.696	16.610	1.00	3.33
	ATOM	575	CG1	VAL	A	77	15.581	-1.252	15.443	1.00	2.00
	ATOM	576	CG2	VAL	A	77	13.484	-2.421	16.081	1.00	3.86
10	ATOM	577	C	VAL	A	77	16.732	-1.934	18.116	1.00	5.20
	ATOM	578	O	VAL	A	77	17.836	-2.200	17.668	1.00	7.18
	ATOM	579	N	GLN	A	78	16.545	-1.112	19.147	1.00	7.90
	ATOM	580	CA	GLN	A	78	17.647	-0.400	19.796	1.00	8.36
	ATOM	581	CB	GLN	A	78	17.104	0.626	20.785	1.00	7.00
15	ATOM	582	CG	GLN	A	78	18.147	1.295	21.662	1.00	7.62
	ATOM	583	CD	GLN	A	78	17.533	2.287	22.608	1.00	7.33
	ATOM	584	OE1	GLN	A	78	16.347	2.220	22.914	1.00	12.26
	ATOM	585	NE2	GLN	A	78	18.328	3.218	23.072	1.00	9.76
	ATOM	586	C	GLN	A	78	18.635	-1.349	20.506	1.00	9.63
20	ATOM	587	O	GLN	A	78	19.841	-1.271	20.253	1.00	9.65
	ATOM	588	N	ASP	A	79	18.138	-2.213	21.400	1.00	8.44
	ATOM	589	CA	ASP	A	79	18.994	-3.177	22.115	1.00	8.37
	ATOM	590	CB	ASP	A	79	18.160	-4.051	23.060	1.00	8.46
	ATOM	591	CG	ASP	A	79	17.514	-3.270	24.188	1.00	8.10
25	ATOM	592	OD1	ASP	A	79	17.933	-2.133	24.478	1.00	10.57
	ATOM	593	OD2	ASP	A	79	16.588	-3.814	24.812	1.00	8.80
	ATOM	594	C	ASP	A	79	19.745	-4.093	21.148	1.00	7.97
	ATOM	595	O	ASP	A	79	20.932	-4.375	21.329	1.00	6.78
	ATOM	596	N	ASN	A	80	19.041	-4.498	20.089	1.00	8.48
30	ATOM	597	CA	ASN	A	80	19.539	-5.396	19.041	1.00	5.82
	ATOM	598	CB	ASN	A	80	18.338	-5.974	18.272	1.00	4.43
	ATOM	599	CG	ASN	A	80	18.725	-7.085	17.345	1.00	3.01
	ATOM	600	OD1	ASN	A	80	18.482	-7.028	16.139	1.00	4.09
	ATOM	601	ND2	ASN	A	80	19.337	-8.107	17.899	1.00	2.84
35	ATOM	602	C	ASN	A	80	20.523	-4.770	18.054	1.00	4.96
	ATOM	603	O	ASN	A	80	21.316	-5.469	17.425	1.00	5.58
	ATOM	604	N	GLY	A	81	20.416	-3.457	17.875	1.00	5.05

ATOM	605	CA	GLY A	81	21.287	-2.755	16.969	1.00	2.00
ATOM	606	C	GLY A	81	20.883	-2.967	15.539	1.00	2.53
ATOM	607	O	GLY A	81	21.726	-2.876	14.642	1.00	2.18
ATOM	608	N	GLY A	82	19.609	-3.278	15.308	1.00	2.00
5 ATOM	609	CA	GLY A	82	19.163	-3.494	13.946	1.00	2.74
ATOM	610	C	GLY A	82	17.855	-4.243	13.852	1.00	3.52
ATOM	611	O	GLY A	82	17.306	-4.685	14.879	1.00	3.74
ATOM	612	N	ILE A	83	17.375	-4.389	12.616	1.00	2.73
ATOM	613	CA	ILE A	83	16.120	-5.076	12.295	1.00	6.15
10 ATOM	614	CB	ILE A	83	14.854	-4.145	12.584	1.00	6.32
ATOM	615	CG2	ILE A	83	14.908	-2.893	11.784	1.00	9.06
ATOM	616	CG1	ILE A	83	13.523	-4.879	12.374	1.00	6.49
ATOM	617	CD1	ILE A	83	13.176	-5.771	13.522	1.00	5.60
ATOM	618	C	ILE A	83	16.241	-5.441	10.819	1.00	5.04
15 ATOM	619	O	ILE A	83	16.659	-4.612	10.028	1.00	6.44
ATOM	620	N	ASP A	84	15.964	-6.702	10.463	1.00	5.67
ATOM	621	CA	ASP A	84	16.081	-7.152	9.072	1.00	5.79
ATOM	622	CB	ASP A	84	16.131	-8.690	8.965	1.00	6.39
ATOM	623	CG	ASP A	84	17.361	-9.291	9.626	1.00	7.46
20 ATOM	624	OD1	ASP A	84	18.440	-8.668	9.610	1.00	8.44
ATOM	625	OD2	ASP A	84	17.259	-10.407	10.167	1.00	7.67
ATOM	626	C	ASP A	84	14.949	-6.653	8.223	1.00	6.09
ATOM	627	O	ASP A	84	13.901	-6.238	8.731	1.00	7.75
ATOM	628	N	SER A	85	15.161	-6.701	6.917	1.00	6.34
25 ATOM	629	CA	SER A	85	14.150	-6.294	5.963	1.00	7.18
ATOM	630	CB	SER A	85	14.800	-6.046	4.598	1.00	7.55
ATOM	631	OG	SER A	85	15.465	-7.209	4.130	1.00	9.24
ATOM	632	C	SER A	85	13.057	-7.370	5.838	1.00	7.67
ATOM	633	O	SER A	85	13.266	-8.539	6.180	1.00	7.18
30 ATOM	634	N	GLU A	86	11.884	-6.952	5.380	1.00	5.49
ATOM	635	CA	GLU A	86	10.763	-7.838	5.173	1.00	6.04
ATOM	636	CB	GLU A	86	9.578	-7.046	4.600	1.00	5.74
ATOM	637	CG	GLU A	86	8.282	-7.847	4.425	1.00	4.00
ATOM	638	CD	GLU A	86	7.547	-8.038	5.714	1.00	5.24
35 ATOM	639	OE1	GLU A	86	6.788	-7.128	6.077	1.00	6.23
ATOM	640	OE2	GLU A	86	7.711	-9.084	6.379	1.00	6.50
ATOM	641	C	GLU A	86	11.199	-8.919	4.173	1.00	7.54

	ATOM	642	O	GLU	A	86	10.856	-10.096	4.324	1.00	6.89
	ATOM	643	N	GLU	A	87	11.952	-8.506	3.156	1.00	9.17
	ATOM	644	CA	GLU	A	87	12.439	-9.408	2.126	1.00	9.73
	ATOM	645	CB	GLU	A	87	13.196	-8.630	1.053	1.00	12.02
5	ATOM	646	CG	GLU	A	87	13.623	-9.477	-0.118	1.00	15.12
	ATOM	647	CD	GLU	A	87	14.459	-8.724	-1.131	1.00	18.16
	ATOM	648	OE1	GLU	A	87	14.230	-7.516	-1.339	1.00	21.29
	ATOM	649	OE2	GLU	A	87	15.344	-9.350	-1.740	1.00	19.92
	ATOM	650	C	GLU	A	87	13.331	-10.519	2.670	1.00	9.79
10	ATOM	651	O	GLU	A	87	13.149	-11.669	2.322	1.00	10.68
	ATOM	652	N	SER	A	88	14.285	-10.173	3.528	1.00	10.39
	ATOM	653	CA	SER	A	88	15.218	-11.156	4.093	1.00	9.48
	ATOM	654	CB	SER	A	88	16.469	-10.443	4.640	1.00	8.86
	ATOM	655	OG	SER	A	88	16.239	-9.825	5.907	1.00	7.26
15	ATOM	656	C	SER	A	88	14.643	-12.051	5.196	1.00	8.73
	ATOM	657	O	SER	A	88	15.146	-13.151	5.430	1.00	7.49
	ATOM	658	N	TYR	A	89	13.590	-11.576	5.858	1.00	7.24
	ATOM	659	CA	TYR	A	89	12.978	-12.275	6.983	1.00	6.63
	ATOM	660	CB	TYR	A	89	13.493	-11.594	8.255	1.00	3.81
20	ATOM	661	CG	TYR	A	89	13.514	-12.421	9.506	1.00	3.65
	ATOM	662	CD1	TYR	A	89	14.351	-12.070	10.567	1.00	3.02
	ATOM	663	CE1	TYR	A	89	14.291	-12.749	11.779	1.00	4.19
	ATOM	664	CD2	TYR	A	89	12.631	-13.484	9.687	1.00	3.12
	ATOM	665	CE2	TYR	A	89	12.567	-14.166	10.896	1.00	2.69
25	ATOM	666	CZ	TYR	A	89	13.386	-13.795	11.935	1.00	2.60
	ATOM	667	OH	TYR	A	89	13.276	-14.448	13.150	1.00	4.48
	ATOM	668	C	TYR	A	89	11.436	-12.191	6.856	1.00	6.38
	ATOM	669	O	TYR	A	89	10.751	-11.521	7.640	1.00	6.58
	ATOM	670	N	PRO	A	90	10.873	-12.960	5.913	1.00	6.37
30	ATOM	671	CD	PRO	A	90	11.642	-14.007	5.220	1.00	5.17
	ATOM	672	CA	PRO	A	90	9.446	-13.055	5.582	1.00	6.11
	ATOM	673	CB	PRO	A	90	9.404	-14.185	4.542	1.00	6.13
	ATOM	674	CG	PRO	A	90	10.821	-14.238	3.999	1.00	7.30
	ATOM	675	C	PRO	A	90	8.525	-13.362	6.758	1.00	6.07
35	ATOM	676	O	PRO	A	90	8.938	-13.986	7.734	1.00	7.91
	ATOM	677	N	TYR	A	91	7.261	-12.957	6.630	1.00	5.44
	ATOM	678	CA	TYR	A	91	6.257	-13.166	7.672	1.00	5.59

ATOM	679	CB	TYR	A	91	5.160	-12.088	7.564	1.00	2.92
ATOM	680	CG	TYR	A	91	4.164	-12.078	8.723	1.00	2.95
ATOM	681	CD1	TYR	A	91	4.587	-11.894	10.037	1.00	2.56
ATOM	682	CE1	TYR	A	91	3.685	-11.911	11.093	1.00	2.00
5 ATOM	683	CD2	TYR	A	91	2.809	-12.274	8.500	1.00	3.84
ATOM	684	CE2	TYR	A	91	1.916	-12.280	9.544	1.00	2.44
ATOM	685	CZ	TYR	A	91	2.362	-12.101	10.825	1.00	2.00
ATOM	686	OH	TYR	A	91	1.472	-12.104	11.831	1.00	2.00
ATOM	687	C	TYR	A	91	5.647	-14.583	7.591	1.00	6.55
10 ATOM	688	O	TYR	A	91	5.337	-15.061	6.514	1.00	7.52
ATOM	689	N	GLU	A	92	5.479	-15.237	8.740	1.00	9.38
ATOM	690	CA	GLU	A	92	4.932	-16.588	8.822	1.00	9.85
ATOM	691	CB	GLU	A	92	5.930	-17.527	9.495	1.00	12.09
ATOM	692	CG	GLU	A	92	7.225	-17.762	8.765	1.00	16.86
15 ATOM	693	CD	GLU	A	92	8.076	-18.800	9.474	1.00	18.98
ATOM	694	OE1	GLU	A	92	7.797	-20.011	9.317	1.00	21.96
ATOM	695	OE2	GLU	A	92	9.011	-18.408	10.202	1.00	20.31
ATOM	696	C	GLU	A	92	3.661	-16.662	9.642	1.00	9.18
ATOM	697	O	GLU	A	92	3.032	-17.711	9.693	1.00	10.24
20 ATOM	698	N	ALA	A	93	3.334	-15.587	10.347	1.00	7.87
ATOM	699	CA	ALA	A	93	2.147	-15.537	11.201	1.00	7.08
ATOM	700	CB	ALA	A	93	0.854	-15.664	10.375	1.00	4.50
ATOM	701	C	ALA	A	93	2.181	-16.568	12.323	1.00	6.62
ATOM	702	O	ALA	A	93	1.152	-17.029	12.800	1.00	9.78
25 ATOM	703	N	THR	A	94	3.376	-16.918	12.763	1.00	8.44
ATOM	704	CA	THR	A	94	3.545	-17.846	13.883	1.00	11.70
ATOM	705	CB	THR	A	94	3.692	-19.320	13.417	1.00	11.68
ATOM	706	OG1	THR	A	94	4.774	-19.414	12.479	1.00	12.05
ATOM	707	CG2	THR	A	94	2.416	-19.801	12.752	1.00	13.27
30 ATOM	708	C	THR	A	94	4.825	-17.430	14.620	1.00	12.43
ATOM	709	O	THR	A	94	5.718	-16.810	14.024	1.00	13.81
ATOM	710	N	GLN	A	95	4.888	-17.705	15.915	1.00	13.02
ATOM	711	CA	GLN	A	95	6.066	-17.361	16.690	1.00	15.16
ATOM	712	CB	GLN	A	95	5.711	-17.195	18.173	1.00	16.05
35 ATOM	713	CG	GLN	A	95	6.850	-16.641	19.033	1.00	17.89
ATOM	714	CD	GLN	A	95	6.479	-16.486	20.499	1.00	19.00
ATOM	715	OE1	GLN	A	95	5.300	-16.459	20.852	1.00	21.94

	ATOM	716	NE2	GLN	A	95	7.480	-16.337	21.350	1.00	19.03
	ATOM	717	C	GLN	A	95	7.076	-18.489	16.487	1.00	16.17
	ATOM	718	O	GLN	A	95	6.751	-19.665	16.653	1.00	18.04
	ATOM	719	N	GLU	A	96	8.281	-18.131	16.072	1.00	14.18
5	ATOM	720	CA	GLU	A	96	9.330	-19.105	15.826	1.00	13.91
	ATOM	721	CB	GLU	A	96	9.640	-19.144	14.325	1.00	15.91
	ATOM	722	CG	GLU	A	96	8.500	-19.654	13.423	1.00	18.09
	ATOM	723	CD	GLU	A	96	8.068	-21.079	13.750	1.00	18.52
	ATOM	724	OE1	GLU	A	96	8.940	-21.958	13.943	1.00	19.16
10	ATOM	725	OE2	GLU	A	96	6.842	-21.309	13.828	1.00	20.01
	ATOM	726	C	GLU	A	96	10.579	-18.700	16.603	1.00	12.33
	ATOM	727	O	GLU	A	96	10.538	-17.747	17.363	1.00	12.46
	ATOM	728	N	SER	A	97	11.671	-19.438	16.439	1.00	10.38
	ATOM	729	CA	SER	A	97	12.914	-19.102	17.119	1.00	9.59
15	ATOM	730	CB	SER	A	97	13.895	-20.286	17.092	1.00	10.52
	ATOM	731	OG	SER	A	97	14.427	-20.483	15.788	1.00	12.03
	ATOM	732	C	SER	A	97	13.522	-17.912	16.362	1.00	8.39
	ATOM	733	O	SER	A	97	13.402	-17.817	15.146	1.00	8.25
	ATOM	734	N	CYS	A	98	14.209	-17.037	17.072	1.00	7.78
20	ATOM	735	CA	CYS	A	98	14.806	-15.860	16.458	1.00	7.77
	ATOM	736	C	CYS	A	98	15.866	-16.156	15.393	1.00	8.99
	ATOM	737	O	CYS	A	98	16.832	-16.876	15.661	1.00	7.60
	ATOM	738	CB	CYS	A	98	15.391	-14.959	17.562	1.00	8.37
	ATOM	739	SG	CYS	A	98	16.104	-13.391	16.965	1.00	7.51
25	ATOM	740	N	LYS	A	99	15.692	-15.582	14.200	1.00	7.98
	ATOM	741	CA	LYS	A	99	16.632	-15.766	13.081	1.00	9.08
	ATOM	742	CB	LYS	A	99	15.932	-16.447	11.887	1.00	9.56
	ATOM	743	CG	LYS	A	99	15.268	-17.781	12.214	1.00	11.70
	ATOM	744	CD	LYS	A	99	14.297	-18.219	11.120	1.00	11.75
30	ATOM	745	CE	LYS	A	99	13.536	-19.459	11.539	1.00	12.41
	ATOM	746	NZ	LYS	A	99	12.876	-19.306	12.863	1.00	9.94
	ATOM	747	C	LYS	A	99	17.243	-14.436	12.603	1.00	8.47
	ATOM	748	O	LYS	A	99	17.507	-14.246	11.409	1.00	8.50
	ATOM	749	N	TYR	A	100	17.435	-13.503	13.525	1.00	8.01
35	ATOM	750	CA	TYR	A	100	18.007	-12.213	13.180	1.00	8.06
	ATOM	751	CB	TYR	A	100	17.989	-11.260	14.384	1.00	6.33
	ATOM	752	CG	TYR	A	100	18.754	-9.974	14.101	1.00	5.91

	ATOM	753	CD1	TYR	A	100	18.308	-9.061	13.130	1.00	6.84
	ATOM	754	CE1	TYR	A	100	19.042	-7.897	12.835	1.00	7.37
	ATOM	755	CD2	TYR	A	100	19.938	-9.697	14.762	1.00	4.55
	ATOM	756	CE2	TYR	A	100	20.673	-8.547	14.479	1.00	6.62
5	ATOM	757	CZ	TYR	A	100	20.226	-7.652	13.527	1.00	6.16
	ATOM	758	OH	TYR	A	100	20.961	-6.515	13.299	1.00	6.06
	ATOM	759	C	TYR	A	100	19.444	-12.368	12.700	1.00	8.31
	ATOM	760	O	TYR	A	100	20.244	-13.051	13.340	1.00	10.14
	ATOM	761	N	ASN	A	101	19.766	-11.702	11.599	1.00	9.40
10	ATOM	762	CA	ASN	A	101	21.107	-11.726	11.034	1.00	11.49
	ATOM	763	CB	ASN	A	101	21.107	-12.508	9.705	1.00	12.69
	ATOM	764	CG	ASN	A	101	22.523	-12.795	9.159	1.00	12.49
	ATOM	765	OD1	ASN	A	101	22.691	-13.618	8.270	1.00	14.39
	ATOM	766	ND2	ASN	A	101	23.523	-12.111	9.676	1.00	12.32
15	ATOM	767	C	ASN	A	101	21.502	-10.271	10.791	1.00	11.92
	ATOM	768	O	ASN	A	101	20.835	-9.571	10.038	1.00	12.70
	ATOM	769	N	PRO	A	102	22.597	-9.800	11.427	1.00	13.21
	ATOM	770	CD	PRO	A	102	23.429	-10.561	12.382	1.00	13.68
	ATOM	771	CA	PRO	A	102	23.093	-8.422	11.282	1.00	14.35
20	ATOM	772	CB	PRO	A	102	24.413	-8.447	12.068	1.00	14.93
	ATOM	773	CG	PRO	A	102	24.190	-9.480	13.113	1.00	14.61
	ATOM	774	C	PRO	A	102	23.352	-8.022	9.823	1.00	15.86
	ATOM	775	O	PRO	A	102	23.165	-6.874	9.435	1.00	14.62
	ATOM	776	N	LYS	A	103	23.790	-8.987	9.025	1.00	16.95
25	ATOM	777	CA	LYS	A	103	24.107	-8.764	7.617	1.00	18.84
	ATOM	778	CB	LYS	A	103	24.622	-10.069	7.006	1.00	19.74
	ATOM	779	CG	LYS	A	103	24.913	-10.027	5.520	1.00	20.69
	ATOM	780	CD	LYS	A	103	25.891	-11.136	5.170	1.00	23.17
	ATOM	781	CE	LYS	A	103	25.733	-11.617	3.747	1.00	24.09
30	ATOM	782	NZ	LYS	A	103	24.445	-12.343	3.588	1.00	25.55
	ATOM	783	C	LYS	A	103	22.961	-8.206	6.777	1.00	17.53
	ATOM	784	O	LYS	A	103	23.188	-7.536	5.771	1.00	18.99
	ATOM	785	N	TYR	A	104	21.735	-8.465	7.209	1.00	16.09
	ATOM	786	CA	TYR	A	104	20.547	-8.015	6.497	1.00	13.93
35	ATOM	787	CB	TYR	A	104	19.631	-9.226	6.265	1.00	17.19
	ATOM	788	CG	TYR	A	104	20.233	-10.289	5.368	1.00	18.52
	ATOM	789	CD1	TYR	A	104	20.715	-11.497	5.891	1.00	20.01

ATOM	790	CE1	TYR	A	104	21.272	-12.488	5.041	1.00	20.46
ATOM	791	CD2	TYR	A	104	20.320	-10.085	3.992	1.00	18.97
ATOM	792	CE2	TYR	A	104	20.867	-11.048	3.149	1.00	21.11
ATOM	793	CZ	TYR	A	104	21.341	-12.247	3.670	1.00	21.22
5 ATOM	794	OH	TYR	A	104	21.858	-13.186	2.797	1.00	22.83
ATOM	795	C	TYR	A	104	19.774	-6.894	7.215	1.00	12.09
ATOM	796	O	TYR	A	104	18.623	-6.611	6.870	1.00	11.05
ATOM	797	N	SER	A	105	20.393	-6.286	8.226	1.00	10.05
ATOM	798	CA	SER	A	105	19.774	-5.212	8.989	1.00	10.12
10 ATOM	799	CB	SER	A	105	20.592	-4.935	10.246	1.00	10.22
ATOM	800	OG	SER	A	105	19.972	-3.966	11.069	1.00	13.32
ATOM	801	C	SER	A	105	19.660	-3.957	8.115	1.00	10.60
ATOM	802	O	SER	A	105	20.635	-3.513	7.520	1.00	10.42
ATOM	803	N	VAL	A	106	18.459	-3.392	8.026	1.00	11.25
15 ATOM	804	CA	VAL	A	106	18.229	-2.222	7.186	1.00	8.73
ATOM	805	CB	VAL	A	106	17.268	-2.551	6.038	1.00	9.27
ATOM	806	CG1	VAL	A	106	17.970	-3.393	4.967	1.00	9.09
ATOM	807	CG2	VAL	A	106	16.039	-3.257	6.587	1.00	7.79
ATOM	808	C	VAL	A	106	17.655	-1.036	7.945	1.00	8.47
20 ATOM	809	O	VAL	A	106	17.406	0.013	7.374	1.00	7.49
ATOM	810	N	ALA	A	107	17.472	-1.187	9.243	1.00	9.35
ATOM	811	CA	ALA	A	107	16.909	-0.113	10.024	1.00	7.88
ATOM	812	CB	ALA	A	107	15.390	-0.239	10.045	1.00	9.12
ATOM	813	C	ALA	A	107	17.472	-0.219	11.416	1.00	8.09
25 ATOM	814	O	ALA	A	107	18.091	-1.228	11.748	1.00	7.87
ATOM	815	N	ASN	A	108	17.326	0.849	12.192	1.00	6.12
ATOM	816	CA	ASN	A	108	17.791	0.887	13.569	1.00	8.13
ATOM	817	CB	ASN	A	108	19.330	1.046	13.632	1.00	9.44
ATOM	818	CG	ASN	A	108	19.928	0.521	14.941	1.00	11.94
30 ATOM	819	OD1	ASN	A	108	19.209	0.130	15.878	1.00	10.93
ATOM	820	ND2	ASN	A	108	21.254	0.480	15.001	1.00	14.47
ATOM	821	C	ASN	A	108	17.109	2.075	14.241	1.00	7.01
ATOM	822	O	ASN	A	108	16.512	2.912	13.569	1.00	7.52
ATOM	823	N	ASP	A	109	17.092	2.085	15.564	1.00	6.13
35 ATOM	824	CA	ASP	A	109	16.510	3.200	16.274	1.00	5.45
ATOM	825	CB	ASP	A	109	14.966	3.170	16.292	1.00	3.96
ATOM	826	CG	ASP	A	109	14.376	2.083	17.150	1.00	2.00

	ATOM	827	OD1	ASP	A	109	14.779	1.877	18.307	1.00	2.00
	ATOM	828	OD2	ASP	A	109	13.421	1.471	16.669	1.00	6.11
	ATOM	829	C	ASP	A	109	17.192	3.358	17.627	1.00	6.97
	ATOM	830	O	ASP	A	109	17.946	2.476	18.041	1.00	5.45
5	ATOM	831	N	THR	A	110	17.063	4.552	18.209	1.00	7.11
	ATOM	832	CA	THR	A	110	17.696	4.899	19.473	1.00	6.66
	ATOM	833	CB	THR	A	110	18.530	6.197	19.288	1.00	8.79
	ATOM	834	OG1	THR	A	110	17.690	7.243	18.765	1.00	10.79
	ATOM	835	CG2	THR	A	110	19.686	5.948	18.294	1.00	7.34
10	ATOM	836	C	THR	A	110	16.718	5.066	20.628	1.00	4.62
	ATOM	837	O	THR	A	110	17.040	5.672	21.651	1.00	5.93
	ATOM	838	N	GLY	A	111	15.534	4.493	20.468	1.00	3.74
	ATOM	839	CA	GLY	A	111	14.520	4.596	21.488	1.00	2.67
	ATOM	840	C	GLY	A	111	13.192	4.986	20.884	1.00	2.00
15	ATOM	841	O	GLY	A	111	12.893	4.724	19.735	1.00	2.70
	ATOM	842	N	PHE	A	112	12.362	5.626	21.671	1.00	4.56
	ATOM	843	CA	PHE	A	112	11.062	6.011	21.178	1.00	5.16
	ATOM	844	CB	PHE	A	112	10.088	4.841	21.343	1.00	4.13
	ATOM	845	CG	PHE	A	112	10.111	4.234	22.711	1.00	4.90
20	ATOM	846	CD1	PHE	A	112	9.210	4.650	23.688	1.00	3.88
	ATOM	847	CD2	PHE	A	112	11.054	3.254	23.031	1.00	5.14
	ATOM	848	CE1	PHE	A	112	9.240	4.116	24.949	1.00	4.07
	ATOM	849	CE2	PHE	A	112	11.099	2.705	24.292	1.00	4.00
	ATOM	850	CZ	PHE	A	112	10.194	3.134	25.262	1.00	6.43
25	ATOM	851	C	PHE	A	112	10.570	7.228	21.937	1.00	5.13
	ATOM	852	O	PHE	A	112	11.104	7.591	22.994	1.00	4.21
	ATOM	853	N	VAL	A	113	9.544	7.849	21.379	1.00	6.86
	ATOM	854	CA	VAL	A	113	8.939	9.027	21.962	1.00	5.63
	ATOM	855	CB	VAL	A	113	9.097	10.241	21.002	1.00	5.64
30	ATOM	856	CG1	VAL	A	113	8.347	11.460	21.525	1.00	5.46
	ATOM	857	CG2	VAL	A	113	10.563	10.556	20.801	1.00	2.00
	ATOM	858	C	VAL	A	113	7.469	8.737	22.181	1.00	4.33
	ATOM	859	O	VAL	A	113	6.783	8.356	21.253	1.00	6.32
	ATOM	860	N	ASP	A	114	7.022	8.804	23.425	1.00	2.00
35	ATOM	861	CA	ASP	A	114	5.618	8.602	23.750	1.00	2.83
	ATOM	862	CB	ASP	A	114	5.458	8.046	25.178	1.00	3.20
	ATOM	863	CG	ASP	A	114	5.817	6.549	25.286	1.00	3.67

	ATOM	864	OD1	ASP	A	114	5.806	5.838	24.262	1.00	3.11
	ATOM	865	OD2	ASP	A	114	6.080	6.080	26.406	1.00	6.65
	ATOM	866	C	ASP	A	114	4.918	9.976	23.637	1.00	4.44
	ATOM	867	O	ASP	A	114	5.354	10.961	24.232	1.00	2.19
5	ATOM	868	N	ILE	A	115	3.847	10.039	22.853	1.00	6.03
	ATOM	869	CA	ILE	A	115	3.101	11.285	22.652	1.00	5.07
	ATOM	870	CB	ILE	A	115	2.382	11.224	21.309	1.00	4.23
	ATOM	871	CG2	ILE	A	115	1.486	12.448	21.094	1.00	5.61
	ATOM	872	CG1	ILE	A	115	3.428	11.123	20.205	1.00	5.06
10	ATOM	873	CD1	ILE	A	115	2.867	10.800	18.908	1.00	7.50
	ATOM	874	C	ILE	A	115	2.121	11.503	23.814	1.00	6.10
	ATOM	875	O	ILE	A	115	1.528	10.549	24.305	1.00	5.98
	ATOM	876	N	PRO	A	116	2.059	12.730	24.378	1.00	6.30
	ATOM	877	CD	PRO	A	116	2.848	13.952	24.111	1.00	5.18
15	ATOM	878	CA	PRO	A	116	1.115	12.930	25.489	1.00	5.18
	ATOM	879	CB	PRO	A	116	1.195	14.443	25.739	1.00	6.41
	ATOM	880	CG	PRO	A	116	2.629	14.761	25.357	1.00	5.36
	ATOM	881	C	PRO	A	116	-0.295	12.466	25.088	1.00	4.51
	ATOM	882	O	PRO	A	116	-0.625	12.406	23.903	1.00	5.58
20	ATOM	883	N	LYS	A	117	-1.118	12.143	26.077	1.00	5.49
	ATOM	884	CA	LYS	A	117	-2.487	11.650	25.856	1.00	7.56
	ATOM	885	CB	LYS	A	117	-2.994	10.896	27.117	1.00	8.77
	ATOM	886	CG	LYS	A	117	-4.399	10.264	26.949	1.00	13.73
	ATOM	887	CD	LYS	A	117	-4.762	9.319	28.085	1.00	18.24
25	ATOM	888	CE	LYS	A	117	-6.085	8.595	27.842	1.00	20.02
	ATOM	889	NZ	LYS	A	117	-6.223	7.470	28.831	1.00	23.28
	ATOM	890	C	LYS	A	117	-3.464	12.769	25.456	1.00	4.15
	ATOM	891	O	LYS	A	117	-4.478	12.986	26.105	1.00	3.78
	ATOM	892	N	GLN	A	118	-3.192	13.408	24.330	1.00	4.63
30	ATOM	893	CA	GLN	A	118	-4.006	14.523	23.854	1.00	2.00
	ATOM	894	CB	GLN	A	118	-3.320	15.848	24.246	1.00	2.19
	ATOM	895	CG	GLN	A	118	-3.156	16.116	25.746	1.00	2.00
	ATOM	896	CD	GLN	A	118	-4.465	16.517	26.381	1.00	2.00
	ATOM	897	OE1	GLN	A	118	-5.451	16.770	25.687	1.00	2.00
35	ATOM	898	NE2	GLN	A	118	-4.487	16.583	27.701	1.00	3.75
	ATOM	899	C	GLN	A	118	-4.097	14.443	22.328	1.00	2.00
	ATOM	900	O	GLN	A	118	-3.067	14.348	21.662	1.00	2.66

ATOM	901	N	GLN A 119	-5.309	14.512	21.771	1.00	2.34
ATOM	902	CA	GLN A 119	-5.472	14.465	20.313	1.00	2.40
ATOM	903	CB	GLN A 119	-6.943	14.372	19.926	1.00	2.69
ATOM	904	CG	GLN A 119	-7.502	12.969	20.122	1.00	3.44
5 ATOM	905	CD	GLN A 119	-8.863	12.793	19.527	1.00	2.00
ATOM	906	OE1	GLN A 119	-9.013	12.378	18.386	1.00	2.00
ATOM	907	NE2	GLN A 119	-9.869	13.108	20.298	1.00	2.00
ATOM	908	C	GLN A 119	-4.782	15.649	19.623	1.00	3.36
ATOM	909	O	GLN A 119	-4.364	15.539	18.462	1.00	5.13
10 ATOM	910	N	LYS A 120	-4.609	16.756	20.347	1.00	2.61
ATOM	911	CA	LYS A 120	-3.911	17.923	19.785	1.00	3.92
ATOM	912	CB	LYS A 120	-4.161	19.204	20.616	1.00	2.00
ATOM	913	CG	LYS A 120	-5.561	19.762	20.445	1.00	2.42
ATOM	914	CD	LYS A 120	-5.637	21.206	20.846	1.00	2.46
15 ATOM	915	CE	LYS A 120	-6.904	21.849	20.283	1.00	3.62
ATOM	916	NZ	LYS A 120	-8.149	21.447	21.007	1.00	2.56
ATOM	917	C	LYS A 120	-2.413	17.618	19.673	1.00	2.00
ATOM	918	O	LYS A 120	-1.776	17.936	18.663	1.00	2.00
ATOM	919	N	ALA A 121	-1.872	16.955	20.688	1.00	2.00
20 ATOM	920	CA	ALA A 121	-0.460	16.584	20.672	1.00	4.18
ATOM	921	CB	ALA A 121	-0.019	16.040	22.027	1.00	2.84
ATOM	922	C	ALA A 121	-0.266	15.545	19.567	1.00	4.14
ATOM	923	O	ALA A 121	0.717	15.597	18.834	1.00	5.32
ATOM	924	N	LEU A 122	-1.221	14.631	19.407	1.00	3.62
25 ATOM	925	CA	LEU A 122	-1.105	13.634	18.350	1.00	3.75
ATOM	926	CB	LEU A 122	-2.198	12.558	18.463	1.00	3.20
ATOM	927	CG	LEU A 122	-2.192	11.487	17.358	1.00	2.55
ATOM	928	CD1	LEU A 122	-0.839	10.769	17.325	1.00	2.00
ATOM	929	CD2	LEU A 122	-3.350	10.508	17.585	1.00	2.00
30 ATOM	930	C	LEU A 122	-1.161	14.306	16.981	1.00	3.37
ATOM	931	O	LEU A 122	-0.415	13.944	16.078	1.00	5.98
ATOM	932	N	MET A 123	-2.008	15.317	16.824	1.00	4.16
ATOM	933	CA	MET A 123	-2.109	15.986	15.524	1.00	4.50
ATOM	934	CB	MET A 123	-3.300	16.967	15.492	1.00	2.00
35 ATOM	935	CG	MET A 123	-3.328	17.826	14.240	1.00	6.09
ATOM	936	SD	MET A 123	-4.804	18.832	14.011	1.00	7.73
ATOM	937	CE	MET A 123	-4.871	19.690	15.533	1.00	11.61

ATOM	938	C	MET A 123	-0.793	16.678	15.145	1.00	4.46
ATOM	939	O	MET A 123	-0.304	16.543	14.024	1.00	4.89
ATOM	940	N	LYS A 124	-0.195	17.380	16.101	1.00	6.80
ATOM	941	CA	LYS A 124	1.069	18.061	15.843	1.00	9.63
5 ATOM	942	CB	LYS A 124	1.492	18.927	17.040	1.00	11.48
ATOM	943	CG	LYS A 124	2.818	19.642	16.823	1.00	13.66
ATOM	944	CD	LYS A 124	3.303	20.297	18.094	1.00	19.45
ATOM	945	CE	LYS A 124	4.791	20.710	17.993	1.00	23.17
ATOM	946	NZ	LYS A 124	5.758	19.550	17.946	1.00	25.70
10 ATOM	947	C	LYS A 124	2.167	17.035	15.520	1.00	9.28
ATOM	948	O	LYS A 124	2.959	17.241	14.597	1.00	9.70
ATOM	949	N	ALA A 125	2.213	15.931	16.267	1.00	7.34
ATOM	950	CA	ALA A 125	3.224	14.914	16.011	1.00	5.80
ATOM	951	CB	ALA A 125	3.195	13.821	17.077	1.00	6.66
15 ATOM	952	C	ALA A 125	3.048	14.323	14.616	1.00	4.87
ATOM	953	O	ALA A 125	4.017	14.223	13.883	1.00	5.44
ATOM	954	N	VAL A 126	1.823	13.988	14.220	1.00	5.20
ATOM	955	CA	VAL A 126	1.600	13.433	12.884	1.00	3.43
ATOM	956	CB	VAL A 126	0.140	12.948	12.668	1.00	3.05
20 ATOM	957	CG1	VAL A 126	-0.046	12.439	11.221	1.00	2.65
ATOM	958	CG2	VAL A 126	-0.196	11.830	13.655	1.00	3.06
ATOM	959	C	VAL A 126	1.939	14.472	11.820	1.00	6.95
ATOM	960	O	VAL A 126	2.379	14.118	10.734	1.00	7.09
ATOM	961	N	ALA A 127	1.703	15.751	12.119	1.00	6.76
25 ATOM	962	CA	ALA A 127	2.005	16.822	11.176	1.00	7.26
ATOM	963	CB	ALA A 127	1.314	18.118	11.603	1.00	7.59
ATOM	964	C	ALA A 127	3.507	17.066	10.990	1.00	5.89
ATOM	965	O	ALA A 127	3.935	17.443	9.912	1.00	6.40
ATOM	966	N	THR A 128	4.308	16.814	12.019	1.00	7.92
30 ATOM	967	CA	THR A 128	5.765	17.052	11.954	1.00	10.10
ATOM	968	CB	THR A 128	6.262	17.948	13.163	1.00	11.96
ATOM	969	OG1	THR A 128	5.849	17.385	14.423	1.00	13.80
ATOM	970	CG2	THR A 128	5.720	19.374	13.052	1.00	13.51
ATOM	971	C	THR A 128	6.734	15.848	11.841	1.00	9.92
35 ATOM	972	O	THR A 128	7.799	15.954	11.224	1.00	11.85
ATOM	973	N	VAL A 129	6.374	14.715	12.431	1.00	6.76
ATOM	974	CA	VAL A 129	7.251	13.538	12.444	1.00	5.98

	ATOM	975	CB	VAL A 129	7.077	12.775	13.803	1.00	6.66
	ATOM	976	CG1	VAL A 129	7.995	11.582	13.878	1.00	7.83
	ATOM	977	CG2	VAL A 129	7.321	13.729	14.978	1.00	3.94
	ATOM	978	C	VAL A 129	7.057	12.579	11.274	1.00	5.16
5	ATOM	979	O	VAL A 129	8.003	12.267	10.536	1.00	3.57
	ATOM	980	N	GLY A 130	5.815	12.128	11.113	1.00	4.51
	ATOM	981	CA	GLY A 130	5.464	11.177	10.071	1.00	4.27
	ATOM	982	C	GLY A 130	4.451	10.202	10.649	1.00	2.84
	ATOM	983	O	GLY A 130	3.725	10.579	11.564	1.00	2.22
10	ATOM	984	N	PRO A 131	4.333	8.965	10.120	1.00	3.68
	ATOM	985	CD	PRO A 131	4.854	8.503	8.828	1.00	2.00
	ATOM	986	CA	PRO A 131	3.371	7.989	10.657	1.00	2.96
	ATOM	987	CB	PRO A 131	3.589	6.769	9.766	1.00	2.00
	ATOM	988	CG	PRO A 131	3.863	7.388	8.476	1.00	2.00
15	ATOM	989	C	PRO A 131	3.644	7.694	12.121	1.00	3.70
	ATOM	990	O	PRO A 131	4.797	7.573	12.539	1.00	4.24
	ATOM	991	N	ILE A 132	2.573	7.620	12.905	1.00	3.90
	ATOM	992	CA	ILE A 132	2.681	7.384	14.337	1.00	4.11
	ATOM	993	CB	ILE A 132	2.049	8.564	15.136	1.00	2.00
20	ATOM	994	CG2	ILE A 132	2.125	8.309	16.617	1.00	2.00
	ATOM	995	CG1	ILE A 132	2.744	9.891	14.786	1.00	2.78
	ATOM	996	CD1	ILE A 132	4.212	9.972	15.139	1.00	2.14
	ATOM	997	C	ILE A 132	1.988	6.094	14.758	1.00	3.87
	ATOM	998	O	ILE A 132	0.860	5.819	14.329	1.00	2.00
25	ATOM	999	N	SER A 133	2.652	5.326	15.619	1.00	4.96
	ATOM	1000	CA	SER A 133	2.075	4.069	16.127	1.00	4.29
	ATOM	1001	CB	SER A 133	3.154	3.144	16.740	1.00	2.00
	ATOM	1002	OG	SER A 133	4.018	2.578	15.753	1.00	2.10
	ATOM	1003	C	SER A 133	1.056	4.431	17.204	1.00	4.66
30	ATOM	1004	O	SER A 133	1.341	5.282	18.050	1.00	2.00
	ATOM	1005	N	VAL A 134	-0.140	3.830	17.144	1.00	4.16
	ATOM	1006	CA	VAL A 134	-1.185	4.086	18.144	1.00	3.52
	ATOM	1007	CB	VAL A 134	-2.257	5.151	17.657	1.00	2.00
	ATOM	1008	CG1	VAL A 134	-1.614	6.480	17.286	1.00	2.31
35	ATOM	1009	CG2	VAL A 134	-3.044	4.626	16.486	1.00	2.00
	ATOM	1010	C	VAL A 134	-1.942	2.787	18.480	1.00	2.44
	ATOM	1011	O	VAL A 134	-1.969	1.863	17.682	1.00	2.81

	ATOM	1012	N	ALA A 135	-2.523	2.720	19.673	1.00	5.76
	ATOM	1013	CA	ALA A 135	-3.318	1.572	20.100	1.00	4.17
	ATOM	1014	CB	ALA A 135	-2.886	1.073	21.492	1.00	3.22
	ATOM	1015	C	ALA A 135	-4.745	2.108	20.143	1.00	4.79
5	ATOM	1016	O	ALA A 135	-4.979	3.233	20.577	1.00	3.61
	ATOM	1017	N	ILE A 136	-5.677	1.333	19.605	1.00	4.86
	ATOM	1018	CA	ILE A 136	-7.073	1.713	19.573	1.00	5.26
	ATOM	1019	CB	ILE A 136	-7.580	1.995	18.112	1.00	5.16
	ATOM	1020	CG2	ILE A 136	-6.956	3.271	17.532	1.00	4.00
10	ATOM	1021	CG1	ILE A 136	-7.283	0.792	17.187	1.00	4.19
	ATOM	1022	CD1	ILE A 136	-8.125	0.762	15.964	1.00	2.00
	ATOM	1023	C	ILE A 136	-7.877	0.539	20.100	1.00	5.77
	ATOM	1024	O	ILE A 136	-7.373	-0.590	20.236	1.00	5.42
	ATOM	1025	N	ASP A 137	-9.126	0.823	20.422	1.00	6.93
15	ATOM	1026	CA	ASP A 137	-10.058	-0.186	20.873	1.00	7.89
	ATOM	1027	CB	ASP A 137	-11.068	0.413	21.858	1.00	7.84
	ATOM	1028	CG	ASP A 137	-12.253	-0.518	22.135	1.00	7.68
	ATOM	1029	OD1	ASP A 137	-12.222	-1.699	21.730	1.00	6.28
	ATOM	1030	OD2	ASP A 137	-13.223	-0.069	22.772	1.00	8.41
20	ATOM	1031	C	ASP A 137	-10.768	-0.642	19.601	1.00	6.71
	ATOM	1032	O	ASP A 137	-11.595	0.075	19.061	1.00	9.07
	ATOM	1033	N	ALA A 138	-10.378	-1.811	19.100	1.00	6.39
	ATOM	1034	CA	ALA A 138	-10.968	-2.415	17.902	1.00	5.19
	ATOM	1035	CB	ALA A 138	-9.851	-2.929	17.020	1.00	4.89
25	ATOM	1036	C	ALA A 138	-11.905	-3.580	18.269	1.00	4.07
	ATOM	1037	O	ALA A 138	-12.399	-4.285	17.405	1.00	5.91
	ATOM	1038	N	GLY A 139	-12.148	-3.772	19.562	1.00	5.00
	ATOM	1039	CA	GLY A 139	-12.969	-4.881	20.006	1.00	3.58
	ATOM	1040	C	GLY A 139	-14.465	-4.785	19.849	1.00	3.51
30	ATOM	1041	O	GLY A 139	-15.181	-5.031	20.808	1.00	4.90
	ATOM	1042	N	HIS A 140	-14.949	-4.409	18.672	1.00	3.36
	ATOM	1043	CA	HIS A 140	-16.388	-4.317	18.440	1.00	3.34
	ATOM	1044	CB	HIS A 140	-16.900	-2.878	18.608	1.00	2.00
	ATOM	1045	CG	HIS A 140	-16.680	-2.323	19.982	1.00	2.00
35	ATOM	1046	CD2	HIS A 140	-17.465	-2.330	21.081	1.00	2.00
	ATOM	1047	ND1	HIS A 140	-15.472	-1.791	20.378	1.00	3.34
	ATOM	1048	CE1	HIS A 140	-15.515	-1.511	21.670	1.00	2.59

	ATOM	1049	NE2	HIS	A	140	-16.715	-1.829	22.117	1.00	2.18
	ATOM	1050	C	HIS	A	140	-16.636	-4.809	17.043	1.00	3.99
	ATOM	1051	O	HIS	A	140	-15.779	-4.657	16.188	1.00	6.59
	ATOM	1052	N	GLU	A	141	-17.775	-5.450	16.818	1.00	6.39
5	ATOM	1053	CA	GLU	A	141	-18.123	-5.952	15.490	1.00	7.99
	ATOM	1054	CB	GLU	A	141	-19.462	-6.687	15.539	1.00	11.94
	ATOM	1055	CG	GLU	A	141	-19.442	-7.962	16.345	1.00	16.15
	ATOM	1056	CD	GLU	A	141	-18.579	-9.035	15.701	1.00	18.73
	ATOM	1057	OE1	GLU	A	141	-19.093	-9.712	14.788	1.00	20.83
10	ATOM	1058	OE2	GLU	A	141	-17.396	-9.190	16.097	1.00	19.56
	ATOM	1059	C	GLU	A	141	-18.183	-4.857	14.420	1.00	7.26
	ATOM	1060	O	GLU	A	141	-17.936	-5.120	13.258	1.00	6.79
	ATOM	1061	N	SER	A	142	-18.543	-3.637	14.815	1.00	7.82
	ATOM	1062	CA	SER	A	142	-18.613	-2.514	13.879	1.00	7.23
15	ATOM	1063	CB	SER	A	142	-19.015	-1.231	14.616	1.00	8.19
	ATOM	1064	OG	SER	A	142	-18.149	-0.993	15.725	1.00	7.71
	ATOM	1065	C	SER	A	142	-17.260	-2.300	13.203	1.00	5.91
	ATOM	1066	O	SER	A	142	-17.194	-1.939	12.033	1.00	5.91
	ATOM	1067	N	PHE	A	143	-16.181	-2.532	13.945	1.00	5.73
20	ATOM	1068	CA	PHE	A	143	-14.841	-2.353	13.400	1.00	5.63
	ATOM	1069	CB	PHE	A	143	-13.800	-2.245	14.521	1.00	5.11
	ATOM	1070	CG	PHE	A	143	-12.435	-1.852	14.036	1.00	3.97
	ATOM	1071	CD1	PHE	A	143	-12.115	-0.514	13.860	1.00	2.76
	ATOM	1072	CD2	PHE	A	143	-11.468	-2.822	13.771	1.00	2.00
25	ATOM	1073	CE1	PHE	A	143	-10.843	-0.138	13.436	1.00	3.44
	ATOM	1074	CE2	PHE	A	143	-10.203	-2.458	13.349	1.00	3.53
	ATOM	1075	CZ	PHE	A	143	-9.886	-1.110	13.184	1.00	3.18
	ATOM	1076	C	PHE	A	143	-14.507	-3.506	12.460	1.00	6.01
	ATOM	1077	O	PHE	A	143	-14.012	-3.292	11.355	1.00	5.34
30	ATOM	1078	N	LEU	A	144	-14.804	-4.726	12.891	1.00	7.20
	ATOM	1079	CA	LEU	A	144	-14.539	-5.909	12.070	1.00	8.00
	ATOM	1080	CB	LEU	A	144	-15.002	-7.176	12.809	1.00	9.33
	ATOM	1081	CG	LEU	A	144	-14.691	-8.525	12.151	1.00	10.59
	ATOM	1082	CD1	LEU	A	144	-13.194	-8.661	11.890	1.00	10.40
35	ATOM	1083	CD2	LEU	A	144	-15.177	-9.644	13.050	1.00	9.64
	ATOM	1084	C	LEU	A	144	-15.233	-5.791	10.706	1.00	8.74
	ATOM	1085	O	LEU	A	144	-14.640	-6.077	9.661	1.00	8.65

	ATOM	1086	N	PHE A 145	-16.481	-5.321	10.730	1.00	9.71
	ATOM	1087	CA	PHE A 145	-17.285	-5.153	9.525	1.00	10.03
	ATOM	1088	CB	PHE A 145	-18.721	-5.624	9.789	1.00	9.79
	ATOM	1089	CG	PHE A 145	-18.826	-7.106	9.978	1.00	9.33
5	ATOM	1090	CD1	PHE A 145	-18.931	-7.949	8.877	1.00	9.14
	ATOM	1091	CD2	PHE A 145	-18.728	-7.669	11.250	1.00	10.28
	ATOM	1092	CE1	PHE A 145	-18.925	-9.326	9.037	1.00	8.42
	ATOM	1093	CE2	PHE A 145	-18.719	-9.047	11.423	1.00	9.97
	ATOM	1094	CZ	PHE A 145	-18.817	-9.880	10.308	1.00	8.67
10	ATOM	1095	C	PHE A 145	-17.255	-3.760	8.891	1.00	10.74
	ATOM	1096	O	PHE A 145	-17.996	-3.486	7.947	1.00	12.92
	ATOM	1097	N	TYR A 146	-16.364	-2.903	9.374	1.00	10.25
	ATOM	1098	CA	TYR A 146	-16.211	-1.552	8.840	1.00	10.24
	ATOM	1099	CB	TYR A 146	-15.105	-0.788	9.604	1.00	7.10
15	ATOM	1100	CG	TYR A 146	-14.647	0.469	8.896	1.00	6.36
	ATOM	1101	CD1	TYR A 146	-13.565	0.436	8.022	1.00	5.04
	ATOM	1102	CE1	TYR A 146	-13.185	1.565	7.317	1.00	4.47
	ATOM	1103	CD2	TYR A 146	-15.335	1.679	9.051	1.00	4.80
	ATOM	1104	CE2	TYR A 146	-14.952	2.806	8.354	1.00	2.25
20	ATOM	1105	CZ	TYR A 146	-13.883	2.737	7.498	1.00	2.89
	ATOM	1106	OH	TYR A 146	-13.460	3.832	6.824	1.00	5.77
	ATOM	1107	C	TYR A 146	-15.863	-1.627	7.354	1.00	9.78
	ATOM	1108	O	TYR A 146	-14.991	-2.402	6.957	1.00	9.94
	ATOM	1109	N	ALA A 147	-16.518	-0.792	6.546	1.00	10.69
25	ATOM	1110	CA	ALA A 147	-16.274	-0.766	5.105	1.00	9.95
	ATOM	1111	CB	ALA A 147	-17.504	-1.289	4.335	1.00	9.48
	ATOM	1112	C	ALA A 147	-15.892	0.622	4.601	1.00	10.89
	ATOM	1113	O	ALA A 147	-14.923	0.765	3.856	1.00	12.73
	ATOM	1114	N	GLY A 148	-16.649	1.641	4.999	1.00	10.59
30	ATOM	1115	CA	GLY A 148	-16.354	2.986	4.535	1.00	11.28
	ATOM	1116	C	GLY A 148	-16.821	4.094	5.451	1.00	10.19
	ATOM	1117	O	GLY A 148	-17.563	3.862	6.409	1.00	11.41
	ATOM	1118	N	GLY A 149	-16.337	5.303	5.180	1.00	11.89
	ATOM	1119	CA	GLY A 149	-16.729	6.464	5.963	1.00	9.22
35	ATOM	1120	C	GLY A 149	-15.922	6.671	7.223	1.00	9.50
	ATOM	1121	O	GLY A 149	-14.889	6.047	7.415	1.00	8.92
	ATOM	1122	N	ILE A 150	-16.392	7.575	8.071	1.00	8.68

	ATOM	1123	CA	ILE A 150	-15.730	7.860	9.321	1.00	8.49
	ATOM	1124	CB	ILE A 150	-15.989	9.317	9.771	1.00	7.77
	ATOM	1125	CG2	ILE A 150	-15.408	9.569	11.161	1.00	7.93
	ATOM	1126	CG1	ILE A 150	-15.345	10.283	8.787	1.00	7.43
5	ATOM	1127	CD1	ILE A 150	-15.440	11.716	9.233	1.00	9.23
	ATOM	1128	C	ILE A 150	-16.253	6.866	10.350	1.00	8.25
	ATOM	1129	O	ILE A 150	-17.461	6.803	10.599	1.00	8.91
	ATOM	1130	N	TYR A 151	-15.352	6.037	10.873	1.00	6.97
	ATOM	1131	CA	TYR A 151	-15.708	5.047	11.869	1.00	6.31
10	ATOM	1132	CB	TYR A 151	-14.559	4.038	12.087	1.00	4.18
	ATOM	1133	CG	TYR A 151	-14.824	3.021	13.184	1.00	2.00
	ATOM	1134	CD1	TYR A 151	-15.687	1.943	12.964	1.00	2.93
	ATOM	1135	CE1	TYR A 151	-15.955	1.008	13.967	1.00	2.00
	ATOM	1136	CD2	TYR A 151	-14.225	3.140	14.449	1.00	2.00
15	ATOM	1137	CE2	TYR A 151	-14.481	2.214	15.461	1.00	2.12
	ATOM	1138	CZ	TYR A 151	-15.359	1.142	15.206	1.00	2.70
	ATOM	1139	OH	TYR A 151	-15.654	0.216	16.179	1.00	3.04
	ATOM	1140	C	TYR A 151	-16.016	5.729	13.181	1.00	6.36
	ATOM	1141	O	TYR A 151	-15.200	6.482	13.704	1.00	7.11
20	ATOM	1142	N	PHE A 152	-17.193	5.458	13.717	1.00	6.45
	ATOM	1143	CA	PHE A 152	-17.578	5.993	15.004	1.00	6.30
	ATOM	1144	CB	PHE A 152	-18.461	7.243	14.880	1.00	6.56
	ATOM	1145	CG	PHE A 152	-18.892	7.784	16.206	1.00	8.34
	ATOM	1146	CD1	PHE A 152	-17.972	8.380	17.057	1.00	9.05
25	ATOM	1147	CD2	PHE A 152	-20.196	7.613	16.655	1.00	8.59
	ATOM	1148	CE1	PHE A 152	-18.349	8.784	18.330	1.00	8.82
	ATOM	1149	CE2	PHE A 152	-20.573	8.014	17.924	1.00	6.13
	ATOM	1150	CZ	PHE A 152	-19.658	8.593	18.757	1.00	7.60
	ATOM	1151	C	PHE A 152	-18.320	4.871	15.716	1.00	6.20
30	ATOM	1152	O	PHE A 152	-19.259	4.299	15.174	1.00	6.53
	ATOM	1153	N	GLU A 153	-17.892	4.558	16.926	1.00	6.07
	ATOM	1154	CA	GLU A 153	-18.492	3.491	17.704	1.00	6.66
	ATOM	1155	CB	GLU A 153	-17.494	2.319	17.774	1.00	6.95
	ATOM	1156	CG	GLU A 153	-17.840	1.151	18.702	1.00	7.94
35	ATOM	1157	CD	GLU A 153	-19.263	0.620	18.540	1.00	7.75
	ATOM	1158	OE1	GLU A 153	-19.594	0.045	17.500	1.00	7.60
	ATOM	1159	OE2	GLU A 153	-20.054	0.764	19.488	1.00	11.97

	ATOM	1160	C	GLU A 153	-18.791	4.026	19.087	1.00	7.28
	ATOM	1161	O	GLU A 153	-17.898	4.133	19.915	1.00	10.59
	ATOM	1162	N	PRO A 154	-20.052	4.341	19.375	1.00	7.39
	ATOM	1163	CD	PRO A 154	-21.217	4.180	18.491	1.00	8.01
5	ATOM	1164	CA	PRO A 154	-20.453	4.870	20.679	1.00	8.73
	ATOM	1165	CB	PRO A 154	-21.974	4.997	20.537	1.00	9.35
	ATOM	1166	CG	PRO A 154	-22.324	3.997	19.475	1.00	9.09
	ATOM	1167	C	PRO A 154	-20.050	4.041	21.906	1.00	10.41
	ATOM	1168	O	PRO A 154	-19.930	4.575	23.008	1.00	10.29
10	ATOM	1169	N	ASP A 155	-19.787	2.752	21.695	1.00	12.63
	ATOM	1170	CA	ASP A 155	-19.401	1.838	22.772	1.00	14.09
	ATOM	1171	CB	ASP A 155	-19.993	0.450	22.498	1.00	18.24
	ATOM	1172	CG	ASP A 155	-20.572	-0.203	23.740	1.00	22.25
	ATOM	1173	OD1	ASP A 155	-20.087	0.073	24.866	1.00	24.23
15	ATOM	1174	OD2	ASP A 155	-21.515	-1.011	23.583	1.00	23.87
	ATOM	1175	C	ASP A 155	-17.886	1.718	22.945	1.00	12.31
	ATOM	1176	O	ASP A 155	-17.409	0.985	23.820	1.00	11.49
	ATOM	1177	N	CYS A 156	-17.138	2.448	22.124	1.00	11.10
	ATOM	1178	CA	CYS A 156	-15.673	2.421	22.159	1.00	10.25
20	ATOM	1179	C	CYS A 156	-15.082	2.958	23.463	1.00	11.02
	ATOM	1180	O	CYS A 156	-15.592	3.918	24.037	1.00	13.17
	ATOM	1181	CB	CYS A 156	-15.103	3.204	20.981	1.00	9.79
	ATOM	1182	SG	CYS A 156	-13.922	2.253	19.981	1.00	9.59
	ATOM	1183	N	SER A 157	-13.977	2.357	23.891	1.00	9.16
25	ATOM	1184	CA	SER A 157	-13.286	2.741	25.114	1.00	9.33
	ATOM	1185	CB	SER A 157	-12.870	1.495	25.897	1.00	9.13
	ATOM	1186	OG	SER A 157	-12.026	1.833	26.989	1.00	11.98
	ATOM	1187	C	SER A 157	-12.043	3.573	24.802	1.00	9.01
	ATOM	1188	O	SER A 157	-11.311	3.280	23.851	1.00	7.33
30	ATOM	1189	N	SER A 158	-11.820	4.613	25.598	1.00	11.32
	ATOM	1190	CA	SER A 158	-10.665	5.490	25.437	1.00	12.82
	ATOM	1191	CB	SER A 158	-11.066	6.940	25.756	1.00	12.61
	ATOM	1192	OG	SER A 158	-12.015	7.406	24.807	1.00	14.29
	ATOM	1193	C	SER A 158	-9.526	5.051	26.352	1.00	13.31
35	ATOM	1194	O	SER A 158	-8.454	5.651	26.343	1.00	13.89
	ATOM	1195	N	GLU A 159	-9.751	3.959	27.082	1.00	14.86
	ATOM	1196	CA	GLU A 159	-8.784	3.420	28.047	1.00	17.99

	ATOM	1197	CB	GLU A 159	-9.376	3.507	29.472	1.00	21.62
	ATOM	1198	CG	GLU A 159	-9.327	4.893	30.174	1.00	27.72
	ATOM	1199	CD	GLU A 159	-10.044	6.040	29.431	1.00	31.08
	ATOM	1200	OE1	GLU A 159	-11.217	5.881	29.015	1.00	33.32
5	ATOM	1201	OE2	GLU A 159	-9.431	7.128	29.286	1.00	33.60
	ATOM	1202	C	GLU A 159	-8.336	1.968	27.783	1.00	17.27
	ATOM	1203	O	GLU A 159	-7.237	1.568	28.177	1.00	15.65
	ATOM	1204	N	ASP A 160	-9.201	1.173	27.158	1.00	17.33
	ATOM	1205	CA	ASP A 160	-8.881	-0.224	26.879	1.00	16.78
10	ATOM	1206	CB	ASP A 160	-9.899	-1.163	27.529	1.00	19.87
	ATOM	1207	CG	ASP A 160	-9.660	-1.329	29.020	1.00	22.08
	ATOM	1208	OD1	ASP A 160	-10.537	-0.901	29.801	1.00	23.73
	ATOM	1209	OD2	ASP A 160	-8.594	-1.870	29.416	1.00	24.26
	ATOM	1210	C	ASP A 160	-8.691	-0.567	25.414	1.00	15.82
15	ATOM	1211	O	ASP A 160	-9.548	-1.190	24.770	1.00	15.21
	ATOM	1212	N	MET A 161	-7.536	-0.155	24.911	1.00	12.42
	ATOM	1213	CA	MET A 161	-7.122	-0.395	23.540	1.00	10.56
	ATOM	1214	CB	MET A 161	-5.984	0.566	23.177	1.00	9.97
	ATOM	1215	CG	MET A 161	-6.373	2.052	23.206	1.00	8.93
20	ATOM	1216	SD	MET A 161	-6.388	2.808	24.831	1.00	6.75
	ATOM	1217	CE	MET A 161	-4.613	2.868	25.169	1.00	6.35
	ATOM	1218	C	MET A 161	-6.629	-1.837	23.445	1.00	9.06
	ATOM	1219	O	MET A 161	-6.045	-2.356	24.389	1.00	5.78
	ATOM	1220	N	ASP A 162	-6.795	-2.448	22.276	1.00	9.89
25	ATOM	1221	CA	ASP A 162	-6.386	-3.849	22.086	1.00	9.12
	ATOM	1222	CB	ASP A 162	-7.607	-4.773	22.327	1.00	9.68
	ATOM	1223	CG	ASP A 162	-8.753	-4.538	21.324	1.00	10.19
	ATOM	1224	OD1	ASP A 162	-9.690	-5.359	21.283	1.00	12.60
	ATOM	1225	OD2	ASP A 162	-8.717	-3.557	20.560	1.00	9.29
30	ATOM	1226	C	ASP A 162	-5.780	-4.158	20.718	1.00	7.20
	ATOM	1227	O	ASP A 162	-5.447	-5.302	20.419	1.00	7.80
	ATOM	1228	N	HIS A 163	-5.594	-3.129	19.905	1.00	6.08
	ATOM	1229	CA	HIS A 163	-5.101	-3.314	18.550	1.00	5.69
	ATOM	1230	CB	HIS A 163	-6.319	-3.387	17.620	1.00	3.42
35	ATOM	1231	CG	HIS A 163	-5.996	-3.718	16.201	1.00	4.55
	ATOM	1232	CD2	HIS A 163	-6.293	-3.070	15.050	1.00	4.77
	ATOM	1233	ND1	HIS A 163	-5.272	-4.828	15.835	1.00	5.31

	ATOM	1234	CE1	HIS	A	163	-5.128	-4.850	14.525	1.00	3.80
	ATOM	1235	NE2	HIS	A	163	-5.741	-3.796	14.024	1.00	4.91
	ATOM	1236	C	HIS	A	163	-4.177	-2.159	18.164	1.00	5.34
	ATOM	1237	O	HIS	A	163	-4.574	-1.001	18.192	1.00	5.40
5	ATOM	1238	N	GLY	A	164	-2.943	-2.491	17.812	1.00	5.58
	ATOM	1239	CA	GLY	A	164	-1.972	-1.479	17.439	1.00	3.48
	ATOM	1240	C	GLY	A	164	-2.068	-1.253	15.954	1.00	3.74
	ATOM	1241	O	GLY	A	164	-2.004	-2.211	15.174	1.00	3.16
	ATOM	1242	N	VAL	A	165	-2.224	0.010	15.573	1.00	2.32
10	ATOM	1243	CA	VAL	A	165	-2.365	0.410	14.182	1.00	2.00
	ATOM	1244	CB	VAL	A	165	-3.844	0.801	13.844	1.00	2.00
	ATOM	1245	CG1	VAL	A	165	-4.731	-0.468	13.780	1.00	2.00
	ATOM	1246	CG2	VAL	A	165	-4.397	1.772	14.881	1.00	2.00
	ATOM	1247	C	VAL	A	165	-1.403	1.557	13.889	1.00	2.00
15	ATOM	1248	O	VAL	A	165	-0.541	1.864	14.704	1.00	3.95
	ATOM	1249	N	LEU	A	166	-1.540	2.185	12.729	1.00	2.00
	ATOM	1250	CA	LEU	A	166	-0.634	3.252	12.350	1.00	2.00
	ATOM	1251	CB	LEU	A	166	0.312	2.715	11.263	1.00	2.00
	ATOM	1252	CG	LEU	A	166	1.405	3.677	10.812	1.00	2.06
20	ATOM	1253	CD1	LEU	A	166	2.468	3.784	11.906	1.00	2.00
	ATOM	1254	CD2	LEU	A	166	1.993	3.198	9.512	1.00	2.00
	ATOM	1255	C	LEU	A	166	-1.370	4.490	11.815	1.00	2.00
	ATOM	1256	O	LEU	A	166	-2.151	4.381	10.882	1.00	2.91
	ATOM	1257	N	VAL	A	167	-1.124	5.656	12.397	1.00	2.00
25	ATOM	1258	CA	VAL	A	167	-1.742	6.881	11.911	1.00	2.07
	ATOM	1259	CB	VAL	A	167	-1.948	7.930	13.029	1.00	2.33
	ATOM	1260	CG1	VAL	A	167	-2.537	9.230	12.458	1.00	2.00
	ATOM	1261	CG2	VAL	A	167	-2.870	7.396	14.044	1.00	2.00
	ATOM	1262	C	VAL	A	167	-0.813	7.459	10.861	1.00	2.42
30	ATOM	1263	O	VAL	A	167	0.343	7.764	11.149	1.00	4.10
	ATOM	1264	N	VAL	A	168	-1.302	7.556	9.631	1.00	2.00
	ATOM	1265	CA	VAL	A	168	-0.498	8.107	8.561	1.00	2.89
	ATOM	1266	CB	VAL	A	168	-0.455	7.187	7.288	1.00	2.89
	ATOM	1267	CG1	VAL	A	168	-0.099	5.746	7.665	1.00	2.00
35	ATOM	1268	CG2	VAL	A	168	-1.760	7.246	6.501	1.00	2.49
	ATOM	1269	C	VAL	A	168	-0.985	9.515	8.193	1.00	2.09
	ATOM	1270	O	VAL	A	168	-0.454	10.139	7.284	1.00	2.00

	ATOM	1271	N	GLY A 169	-1.995	10.009	8.897	1.00	2.00
	ATOM	1272	CA	GLY A 169	-2.487	11.330	8.575	1.00	2.00
	ATOM	1273	C	GLY A 169	-3.819	11.615	9.207	1.00	3.02
	ATOM	1274	O	GLY A 169	-4.263	10.874	10.087	1.00	2.26
5	ATOM	1275	N	TYR A 170	-4.442	12.711	8.779	1.00	4.13
	ATOM	1276	CA	TYR A 170	-5.739	13.121	9.287	1.00	4.16
	ATOM	1277	CB	TYR A 170	-5.613	13.859	10.631	1.00	7.05
	ATOM	1278	CG	TYR A 170	-4.674	15.062	10.650	1.00	8.77
	ATOM	1279	CD1	TYR A 170	-5.096	16.322	10.221	1.00	9.89
10	ATOM	1280	CE1	TYR A 170	-4.257	17.431	10.313	1.00	9.67
	ATOM	1281	CD2	TYR A 170	-3.380	14.944	11.161	1.00	9.54
	ATOM	1282	CE2	TYR A 170	-2.538	16.043	11.249	1.00	10.90
	ATOM	1283	CZ	TYR A 170	-2.988	17.284	10.827	1.00	10.64
	ATOM	1284	OH	TYR A 170	-2.167	18.367	10.977	1.00	11.05
15	ATOM	1285	C	TYR A 170	-6.426	13.994	8.263	1.00	5.39
	ATOM	1286	O	TYR A 170	-5.820	14.420	7.262	1.00	4.57
	ATOM	1287	N	GLY A 171	-7.703	14.244	8.489	1.00	4.36
	ATOM	1288	CA	GLY A 171	-8.436	15.067	7.556	1.00	5.12
	ATOM	1289	C	GLY A 171	-9.835	15.311	8.051	1.00	5.48
20	ATOM	1290	O	GLY A 171	-10.154	15.080	9.220	1.00	5.50
	ATOM	1291	N	PHE A 172	-10.685	15.725	7.127	1.00	8.43
	ATOM	1292	CA	PHE A 172	-12.073	16.028	7.437	1.00	12.21
	ATOM	1293	CB	PHE A 172	-12.188	17.461	8.015	1.00	10.64
	ATOM	1294	CG	PHE A 172	-11.753	18.511	7.058	1.00	12.04
25	ATOM	1295	CD1	PHE A 172	-12.674	19.079	6.166	1.00	12.73
	ATOM	1296	CD2	PHE A 172	-10.400	18.811	6.913	1.00	10.22
	ATOM	1297	CE1	PHE A 172	-12.241	19.911	5.127	1.00	13.64
	ATOM	1298	CE2	PHE A 172	-9.961	19.631	5.892	1.00	10.76
	ATOM	1299	CZ	PHE A 172	-10.875	20.183	4.989	1.00	11.62
30	ATOM	1300	C	PHE A 172	-12.869	15.898	6.138	1.00	12.68
	ATOM	1301	O	PHE A 172	-12.305	15.964	5.029	1.00	12.32
	ATOM	1302	N	GLU A 173	-14.164	15.649	6.275	1.00	16.06
	ATOM	1303	CA	GLU A 173	-15.032	15.532	5.111	1.00	19.68
	ATOM	1304	CB	GLU A 173	-15.958	14.310	5.238	1.00	21.86
35	ATOM	1305	CG	GLU A 173	-15.252	12.943	5.244	1.00	25.42
	ATOM	1306	CD	GLU A 173	-16.219	11.738	5.208	1.00	27.43
	ATOM	1307	OE1	GLU A 173	-17.371	11.830	5.721	1.00	26.18

	ATOM	1308	OE2	GLU A 173	-15.806	10.683	4.664	1.00	29.03
	ATOM	1309	C	GLU A 173	-15.861	16.814	5.034	1.00	19.87
	ATOM	1310	O	GLU A 173	-16.475	17.209	6.019	1.00	19.21
	ATOM	1311	N	SER A 174	-15.852	17.473	3.879	1.00	21.76
5	ATOM	1312	CA	SER A 174	-16.611	18.709	3.685	1.00	23.39
	ATOM	1313	CB	SER A 174	-16.263	19.326	2.336	1.00	24.50
	ATOM	1314	OG	SER A 174	-15.900	20.691	2.504	1.00	29.61
	ATOM	1315	C	SER A 174	-18.129	18.530	3.798	1.00	23.13
	ATOM	1316	O	SER A 174	-18.731	17.741	3.066	1.00	24.67
10	ATOM	1316	OH	SER A 174	-18.731	19.741	3.066	1.00	24.67
	ATOM	1317	N	ASN B 179	-18.343	16.440	13.685	1.00	29.23
	ATOM	1318	CA	ASN B 179	-18.080	15.003	13.614	1.00	28.13
	ATOM	1319	CB	ASN B 179	-19.293	14.240	14.147	1.00	29.81
	ATOM	1320	CG	ASN B 179	-19.614	14.606	15.594	1.00	30.79
15	ATOM	1321	OD1	ASN B 179	-18.796	15.226	16.289	1.00	30.85
	ATOM	1322	ND2	ASN B 179	-20.804	14.226	16.057	1.00	31.47
	ATOM	1323	C	ASN B 179	-17.791	14.671	12.158	1.00	26.17
	ATOM	1324	O	ASN B 179	-18.385	13.764	11.553	1.00	27.58
	ATOM	1325	N	ASN B 180	-16.898	15.479	11.593	1.00	23.23
20	ATOM	1326	CA	ASN B 180	-16.475	15.365	10.204	1.00	18.57
	ATOM	1327	CB	ASN B 180	-16.935	16.598	9.420	1.00	18.84
	ATOM	1328	CG	ASN B 180	-16.057	17.815	9.680	1.00	17.60
	ATOM	1329	OD1	ASN B 180	-15.578	18.027	10.796	1.00	19.00
	ATOM	1330	ND2	ASN B 180	-15.818	18.597	8.646	1.00	18.32
25	ATOM	1331	C	ASN B 180	-14.948	15.239	10.098	1.00	15.32
	ATOM	1332	O	ASN B 180	-14.395	15.224	8.993	1.00	14.06
	ATOM	1333	N	LYS B 181	-14.262	15.211	11.232	1.00	11.94
	ATOM	1334	CA	LYS B 181	-12.821	15.063	11.189	1.00	11.71
	ATOM	1335	CB	LYS B 181	-12.155	16.013	12.188	1.00	11.39
30	ATOM	1336	CG	LYS B 181	-12.080	17.434	11.640	1.00	12.51
	ATOM	1337	CD	LYS B 181	-11.385	18.400	12.587	1.00	10.42
	ATOM	1338	CE	LYS B 181	-12.228	18.659	13.784	1.00	11.13
	ATOM	1339	NZ	LYS B 181	-11.566	19.675	14.640	1.00	13.87
	ATOM	1340	C	LYS B 181	-12.439	13.592	11.423	1.00	10.20
35	ATOM	1341	O	LYS B 181	-13.179	12.838	12.066	1.00	6.89
	ATOM	1342	N	TYR B 182	-11.291	13.187	10.883	1.00	11.29
	ATOM	1343	CA	TYR B 182	-10.816	11.809	11.030	1.00	9.68

	ATOM	1344	CB	TYR B 182	-11.373	10.924	9.896	1.00	8.59
	ATOM	1345	CG	TYR B 182	-10.889	11.299	8.512	1.00	8.36
	ATOM	1346	CD1	TYR B 182	-11.657	12.118	7.686	1.00	8.98
	ATOM	1347	CE1	TYR B 182	-11.217	12.491	6.424	1.00	8.31
5	ATOM	1348	CD2	TYR B 182	-9.657	10.858	8.034	1.00	9.50
	ATOM	1349	CE2	TYR B 182	-9.193	11.237	6.770	1.00	8.86
	ATOM	1350	CZ	TYR B 182	-9.986	12.058	5.968	1.00	10.80
	ATOM	1351	OH	TYR B 182	-9.553	12.454	4.711	1.00	12.63
	ATOM	1352	C	TYR B 182	-9.298	11.693	11.013	1.00	8.23
10	ATOM	1353	O	TYR B 182	-8.597	12.588	10.531	1.00	8.51
	ATOM	1354	N	TRP B 183	-8.827	10.541	11.483	1.00	6.74
	ATOM	1355	CA	TRP B 183	-7.413	10.174	11.492	1.00	5.15
	ATOM	1356	CB	TRP B 183	-6.997	9.471	12.810	1.00	3.98
	ATOM	1357	CG	TRP B 183	-6.971	10.324	14.044	1.00	2.37
15	ATOM	1358	CD2	TRP B 183	-6.030	11.363	14.352	1.00	2.00
	ATOM	1359	CE2	TRP B 183	-6.408	11.918	15.591	1.00	2.08
	ATOM	1360	CE3	TRP B 183	-4.902	11.878	13.690	1.00	2.00
	ATOM	1361	CD1	TRP B 183	-7.857	10.284	15.093	1.00	2.00
	ATOM	1362	NE1	TRP B 183	-7.523	11.240	16.024	1.00	2.18
20	ATOM	1363	CZ2	TRP B 183	-5.702	12.971	16.190	1.00	2.00
	ATOM	1364	CZ3	TRP B 183	-4.200	12.922	14.287	1.00	2.00
	ATOM	1365	CH2	TRP B 183	-4.609	13.456	15.529	1.00	2.00
	ATOM	1366	C	TRP B 183	-7.331	9.141	10.381	1.00	4.37
	ATOM	1367	O	TRP B 183	-8.206	8.290	10.260	1.00	5.30
25	ATOM	1368	N	LEU B 184	-6.336	9.256	9.522	1.00	4.89
	ATOM	1369	CA	LEU B 184	-6.148	8.282	8.467	1.00	5.71
	ATOM	1370	CB	LEU B 184	-5.398	8.914	7.296	1.00	6.57
	ATOM	1371	CG	LEU B 184	-5.366	8.064	6.027	1.00	8.89
	ATOM	1372	CD1	LEU B 184	-6.765	7.619	5.659	1.00	10.53
30	ATOM	1373	CD2	LEU B 184	-4.756	8.862	4.904	1.00	10.66
	ATOM	1374	C	LEU B 184	-5.322	7.166	9.150	1.00	6.28
	ATOM	1375	O	LEU B 184	-4.180	7.386	9.551	1.00	5.46
	ATOM	1376	N	VAL B 185	-5.935	5.995	9.314	1.00	6.48
	ATOM	1377	CA	VAL B 185	-5.318	4.861	10.003	1.00	4.83
35	ATOM	1378	CB	VAL B 185	-6.154	4.518	11.262	1.00	5.57
	ATOM	1379	CG1	VAL B 185	-5.682	3.208	11.916	1.00	6.15
	ATOM	1380	CG2	VAL B 185	-6.095	5.690	12.255	1.00	4.05

	ATOM	1381	C	VAL B 185	-5.070	3.597	9.160	1.00	5.60
	ATOM	1382	O	VAL B 185	-5.996	3.024	8.583	1.00	2.61
	ATOM	1383	N	LYS B 186	-3.792	3.212	9.067	1.00	5.93
	ATOM	1384	CA	LYS B 186	-3.360	2.013	8.348	1.00	5.03
5	ATOM	1385	CB	LYS B 186	-1.898	2.145	7.910	1.00	2.00
	ATOM	1386	CG	LYS B 186	-1.412	0.974	7.058	1.00	3.08
	ATOM	1387	CD	LYS B 186	0.083	1.045	6.833	1.00	2.00
	ATOM	1388	CE	LYS B 186	0.497	0.145	5.694	1.00	2.00
	ATOM	1389	NZ	LYS B 186	1.960	-0.032	5.588	1.00	2.08
10	ATOM	1390	C	LYS B 186	-3.504	0.788	9.265	1.00	3.70
	ATOM	1391	O	LYS B 186	-2.961	0.766	10.368	1.00	3.08
	ATOM	1392	N	ASN B 187	-4.244	-0.221	8.806	1.00	4.50
	ATOM	1393	CA	ASN B 187	-4.448	-1.453	9.584	1.00	3.91
	ATOM	1394	CB	ASN B 187	-5.938	-1.863	9.554	1.00	3.32
15	ATOM	1395	CG	ASN B 187	-6.311	-2.843	10.645	1.00	2.76
	ATOM	1396	OD1	ASN B 187	-5.470	-3.254	11.437	1.00	3.97
	ATOM	1397	ND2	ASN B 187	-7.592	-3.189	10.723	1.00	2.00
	ATOM	1398	C	ASN B 187	-3.565	-2.548	8.959	1.00	3.91
	ATOM	1399	O	ASN B 187	-2.906	-2.320	7.930	1.00	5.02
20	ATOM	1400	N	SER B 188	-3.499	-3.704	9.609	1.00	3.14
	ATOM	1401	CA	SER B 188	-2.715	-4.822	9.106	1.00	3.31
	ATOM	1402	CB	SER B 188	-1.553	-5.142	10.042	1.00	2.00
	ATOM	1403	OG	SER B 188	-1.970	-5.238	11.391	1.00	2.00
	ATOM	1404	C	SER B 188	-3.607	-6.042	8.905	1.00	3.75
25	ATOM	1405	O	SER B 188	-3.233	-7.160	9.245	1.00	3.49
	ATOM	1406	N	TRP B 189	-4.778	-5.808	8.323	1.00	5.44
	ATOM	1407	CA	TRP B 189	-5.745	-6.864	8.036	1.00	6.30
	ATOM	1408	CB	TRP B 189	-7.086	-6.568	8.694	1.00	5.78
	ATOM	1409	CG	TRP B 189	-7.075	-6.721	10.165	1.00	5.36
30	ATOM	1410	CD2	TRP B 189	-8.131	-6.373	11.049	1.00	4.80
	ATOM	1411	CE2	TRP B 189	-7.685	-6.637	12.360	1.00	4.52
	ATOM	1412	CE3	TRP B 189	-9.422	-5.854	10.861	1.00	4.80
	ATOM	1413	CD1	TRP B 189	-6.053	-7.184	10.947	1.00	5.31
	ATOM	1414	NE1	TRP B 189	-6.411	-7.133	12.271	1.00	3.77
35	ATOM	1415	CZ2	TRP B 189	-8.485	-6.396	13.481	1.00	6.20
	ATOM	1416	CZ3	TRP B 189	-10.213	-5.617	11.963	1.00	3.93
	ATOM	1417	CH2	TRP B 189	-9.744	-5.886	13.263	1.00	6.61

	ATOM	1418	C	TRP B 189	-5.940	-7.053	6.533	1.00	6.24
	ATOM	1419	O	TRP B 189	-6.985	-7.530	6.078	1.00	8.03
	ATOM	1420	N	GLY B 190	-4.914	-6.698	5.770	1.00	5.57
	ATOM	1421	CA	GLY B 190	-4.968	-6.857	4.336	1.00	7.76
5	ATOM	1422	C	GLY B 190	-5.709	-5.708	3.710	1.00	9.19
	ATOM	1423	O	GLY B 190	-6.386	-4.955	4.410	1.00	9.35
	ATOM	1424	N	GLU B 191	-5.599	-5.572	2.396	1.00	11.99
	ATOM	1425	CA	GLU B 191	-6.265	-4.477	1.729	1.00	15.41
	ATOM	1426	CB	GLU B 191	-5.491	-3.992	0.494	1.00	18.10
10	ATOM	1427	CG	GLU B 191	-5.680	-4.772	-0.778	1.00	22.38
	ATOM	1428	CD	GLU B 191	-5.576	-3.886	-2.012	1.00	24.80
	ATOM	1429	OE1	GLU B 191	-4.495	-3.292	-2.239	1.00	25.76
	ATOM	1430	OE2	GLU B 191	-6.586	-3.777	-2.750	1.00	25.33
	ATOM	1431	C	GLU B 191	-7.740	-4.671	1.422	1.00	16.08
15	ATOM	1432	O	GLU B 191	-8.378	-3.741	0.963	1.00	18.21
	ATOM	1433	N	GLU B 192	-8.309	-5.838	1.716	1.00	16.39
	ATOM	1434	CA	GLU B 192	-9.731	-6.042	1.439	1.00	17.58
	ATOM	1435	CB	GLU B 192	-10.018	-7.461	0.939	1.00	21.48
	ATOM	1436	CG	GLU B 192	-10.005	-7.608	-0.600	1.00	24.93
20	ATOM	1437	CD	GLU B 192	-8.651	-7.314	-1.229	1.00	27.46
	ATOM	1438	OE1	GLU B 192	-7.663	-8.018	-0.884	1.00	29.01
	ATOM	1439	OE2	GLU B 192	-8.578	-6.387	-2.076	1.00	28.64
	ATOM	1440	C	GLU B 192	-10.622	-5.677	2.619	1.00	15.65
	ATOM	1441	O	GLU B 192	-11.842	-5.779	2.540	1.00	17.05
25	ATOM	1442	N	TRP B 193	-10.000	-5.321	3.735	1.00	12.72
	ATOM	1443	CA	TRP B 193	-10.726	-4.890	4.915	1.00	10.26
	ATOM	1444	CB	TRP B 193	-9.945	-5.205	6.195	1.00	9.01
	ATOM	1445	CG	TRP B 193	-10.609	-4.662	7.418	1.00	6.29
	ATOM	1446	CD2	TRP B 193	-10.359	-3.395	8.043	1.00	6.14
30	ATOM	1447	CE2	TRP B 193	-11.254	-3.282	9.126	1.00	5.42
	ATOM	1448	CE3	TRP B 193	-9.465	-2.342	7.791	1.00	5.54
	ATOM	1449	CD1	TRP B 193	-11.610	-5.250	8.133	1.00	6.47
	ATOM	1450	NE1	TRP B 193	-12.002	-4.428	9.155	1.00	7.53
	ATOM	1451	CZ2	TRP B 193	-11.286	-2.166	9.956	1.00	5.40
35	ATOM	1452	CZ3	TRP B 193	-9.493	-1.234	8.617	1.00	2.49
	ATOM	1453	CH2	TRP B 193	-10.395	-1.152	9.683	1.00	4.22
	ATOM	1454	C	TRP B 193	-10.808	-3.369	4.772	1.00	10.85

	ATOM	1455	O	TRP B 193	-9.881	-2.753	4.238	1.00	11.56
	ATOM	1456	N	GLY B 194	-11.881	-2.773	5.288	1.00	11.54
	ATOM	1457	CA	GLY B 194	-12.047	-1.334	5.232	1.00	9.53
	ATOM	1458	C	GLY B 194	-11.857	-0.749	3.859	1.00	10.38
5	ATOM	1459	O	GLY B 194	-12.201	-1.373	2.845	1.00	12.08
	ATOM	1460	N	MET B 195	-11.281	0.443	3.819	1.00	10.12
	ATOM	1461	CA	MET B 195	-11.051	1.131	2.561	1.00	10.17
	ATOM	1462	CB	MET B 195	-11.234	2.636	2.749	1.00	12.77
	ATOM	1463	CG	MET B 195	-12.577	3.011	3.368	1.00	14.51
10	ATOM	1464	SD	MET B 195	-12.818	4.797	3.503	1.00	15.17
	ATOM	1465	CE	MET B 195	-13.257	5.170	1.846	1.00	12.95
	ATOM	1466	C	MET B 195	-9.650	0.845	2.095	1.00	9.98
	ATOM	1467	O	MET B 195	-8.725	1.596	2.400	1.00	12.23
	ATOM	1468	N	GLY B 196	-9.481	-0.244	1.350	1.00	10.11
15	ATOM	1469	CA	GLY B 196	-8.158	-0.607	0.873	1.00	7.24
	ATOM	1470	C	GLY B 196	-7.198	-0.863	2.020	1.00	5.18
	ATOM	1471	O	GLY B 196	-6.006	-0.613	1.910	1.00	6.22
	ATOM	1472	N	GLY B 197	-7.733	-1.327	3.138	1.00	5.69
	ATOM	1473	CA	GLY B 197	-6.912	-1.612	4.297	1.00	6.35
20	ATOM	1474	C	GLY B 197	-6.801	-0.492	5.310	1.00	5.93
	ATOM	1475	O	GLY B 197	-6.172	-0.666	6.349	1.00	8.00
	ATOM	1476	N	TYR B 198	-7.397	0.655	5.001	1.00	6.76
	ATOM	1477	CA	TYR B 198	-7.387	1.826	5.877	1.00	4.21
	ATOM	1478	CB	TYR B 198	-7.034	3.096	5.085	1.00	3.49
25	ATOM	1479	CG	TYR B 198	-5.574	3.218	4.759	1.00	2.98
	ATOM	1480	CD1	TYR B 198	-4.749	4.060	5.500	1.00	2.00
	ATOM	1481	CE1	TYR B 198	-3.372	4.090	5.287	1.00	2.00
	ATOM	1482	CD2	TYR B 198	-4.997	2.412	3.784	1.00	3.11
	ATOM	1483	CE2	TYR B 198	-3.629	2.432	3.561	1.00	2.79
30	ATOM	1484	CZ	TYR B 198	-2.815	3.270	4.315	1.00	2.98
	ATOM	1485	OH	TYR B 198	-1.450	3.278	4.077	1.00	3.39
	ATOM	1486	C	TYR B 198	-8.752	2.030	6.489	1.00	4.93
	ATOM	1487	O	TYR B 198	-9.758	1.503	6.003	1.00	5.90
	ATOM	1488	N	VAL B 199	-8.777	2.830	7.547	1.00	4.85
35	ATOM	1489	CA	VAL B 199	-9.998	3.172	8.250	1.00	4.01
	ATOM	1490	CB	VAL B 199	-10.297	2.192	9.470	1.00	3.06
	ATOM	1491	CG1	VAL B 199	-9.041	1.972	10.349	1.00	2.46

	ATOM	1492	CG2	VAL	B	199	-11.471	2.709	10.312	1.00	2.00
	ATOM	1493	C	VAL	B	199	-9.854	4.637	8.703	1.00	5.20
	ATOM	1494	O	VAL	B	199	-8.766	5.072	9.113	1.00	5.29
	ATOM	1495	N	LYS	B	200	-10.901	5.422	8.456	1.00	5.99
5	ATOM	1496	CA	LYS	B	200	-10.945	6.824	8.865	1.00	3.79
	ATOM	1497	CB	LYS	B	200	-11.784	7.648	7.889	1.00	4.53
	ATOM	1498	CG	LYS	B	200	-11.142	7.778	6.513	1.00	4.39
	ATOM	1499	CD	LYS	B	200	-11.760	8.851	5.602	1.00	5.37
	ATOM	1500	CE	LYS	B	200	-13.096	8.479	5.057	1.00	6.22
10	ATOM	1501	NZ	LYS	B	200	-13.314	9.154	3.734	1.00	8.43
	ATOM	1502	C	LYS	B	200	-11.588	6.813	10.229	1.00	4.61
	ATOM	1503	O	LYS	B	200	-12.790	6.645	10.334	1.00	6.47
	ATOM	1504	N	MET	B	201	-10.761	6.899	11.272	1.00	5.90
	ATOM	1505	CA	MET	B	201	-11.201	6.880	12.668	1.00	4.43
15	ATOM	1506	CB	MET	B	201	-10.044	6.385	13.553	1.00	6.85
	ATOM	1507	CG	MET	B	201	-9.616	4.921	13.344	1.00	7.98
	ATOM	1508	SD	MET	B	201	-10.856	3.793	13.965	1.00	8.47
	ATOM	1509	CE	MET	B	201	-10.568	3.867	15.739	1.00	7.39
	ATOM	1510	C	MET	B	201	-11.625	8.276	13.131	1.00	3.89
20	ATOM	1511	O	MET	B	201	-10.873	9.222	12.971	1.00	3.07
	ATOM	1512	N	ALA	B	202	-12.803	8.393	13.739	1.00	5.48
	ATOM	1513	CA	ALA	B	202	-13.316	9.677	14.237	1.00	6.98
	ATOM	1514	CB	ALA	B	202	-14.556	9.438	15.120	1.00	6.14
	ATOM	1515	C	ALA	B	202	-12.262	10.477	15.021	1.00	7.19
25	ATOM	1516	O	ALA	B	202	-11.737	10.009	16.036	1.00	8.35
	ATOM	1517	N	LYS	B	203	-11.948	11.672	14.539	1.00	6.08
	ATOM	1518	CA	LYS	B	203	-10.962	12.542	15.173	1.00	3.97
	ATOM	1519	CB	LYS	B	203	-9.991	13.058	14.109	1.00	3.43
	ATOM	1520	CG	LYS	B	203	-8.975	14.096	14.571	1.00	4.08
30	ATOM	1521	CD	LYS	B	203	-7.969	14.367	13.483	1.00	2.00
	ATOM	1522	CE	LYS	B	203	-7.065	15.504	13.866	1.00	3.41
	ATOM	1523	NZ	LYS	B	203	-7.795	16.808	13.845	1.00	3.63
	ATOM	1524	C	LYS	B	203	-11.611	13.712	15.911	1.00	4.66
	ATOM	1525	O	LYS	B	203	-12.626	14.277	15.462	1.00	5.34
35	ATOM	1526	N	ASP	B	204	-11.023	14.033	17.058	1.00	5.46
	ATOM	1527	CA	ASP	B	204	-11.452	15.112	17.938	1.00	8.48
	ATOM	1528	CB	ASP	B	204	-11.312	16.469	17.243	1.00	7.66

	ATOM	1529	CG	ASP B 204	-9.875	16.785	16.879	1.00	5.97
	ATOM	1530	OD1	ASP B 204	-8.983	16.543	17.720	1.00	6.13
	ATOM	1531	OD2	ASP B 204	-9.630	17.246	15.746	1.00	6.01
	ATOM	1532	C	ASP B 204	-12.856	14.908	18.483	1.00	11.09
5	ATOM	1533	O	ASP B 204	-13.639	15.853	18.609	1.00	12.16
	ATOM	1534	N	ARG B 205	-13.155	13.658	18.830	1.00	10.89
	ATOM	1535	CA	ARG B 205	-14.445	13.293	19.386	1.00	8.86
	ATOM	1536	CB	ARG B 205	-15.189	12.392	18.418	1.00	9.96
	ATOM	1537	CG	ARG B 205	-15.660	13.120	17.170	1.00	8.84
10	ATOM	1538	CD	ARG B 205	-16.979	12.543	16.735	1.00	11.03
	ATOM	1539	NE	ARG B 205	-17.925	12.587	17.853	1.00	12.78
	ATOM	1540	CZ	ARG B 205	-19.136	12.044	17.847	1.00	12.72
	ATOM	1541	NH1	ARG B 205	-19.578	11.393	16.779	1.00	14.34
	ATOM	1542	NH2	ARG B 205	-19.919	12.183	18.903	1.00	13.91
15	ATOM	1543	C	ARG B 205	-14.167	12.581	20.691	1.00	10.06
	ATOM	1544	O	ARG B 205	-14.461	11.391	20.848	1.00	9.66
	ATOM	1545	N	ALA B 206	-13.520	13.323	21.590	1.00	7.99
	ATOM	1546	CA	ALA B 206	-13.118	12.871	22.922	1.00	9.48
	ATOM	1547	CB	ALA B 206	-14.334	12.704	23.835	1.00	9.13
20	ATOM	1548	C	ALA B 206	-12.214	11.630	22.976	1.00	8.23
	ATOM	1549	O	ALA B 206	-12.425	10.747	23.793	1.00	8.74
	ATOM	1550	N	ASN B 207	-11.168	11.618	22.147	1.00	7.13
	ATOM	1551	CA	ASN B 207	-10.191	10.521	22.096	1.00	5.29
	ATOM	1552	CB	ASN B 207	-9.439	10.401	23.430	1.00	4.29
25	ATOM	1553	CG	ASN B 207	-8.238	9.470	23.346	1.00	3.56
	ATOM	1554	OD1	ASN B 207	-7.783	9.117	22.252	1.00	5.32
	ATOM	1555	ND2	ASN B 207	-7.711	9.088	24.495	1.00	3.67
	ATOM	1556	C	ASN B 207	-10.902	9.214	21.756	1.00	4.96
	ATOM	1557	O	ASN B 207	-10.786	8.202	22.456	1.00	4.62
30	ATOM	1558	N	HIS B 208	-11.638	9.256	20.658	1.00	5.63
	ATOM	1559	CA	HIS B 208	-12.413	8.117	20.198	1.00	5.79
	ATOM	1560	CB	HIS B 208	-13.133	8.468	18.894	1.00	5.93
	ATOM	1561	CG	HIS B 208	-14.188	7.485	18.515	1.00	6.32
	ATOM	1562	CD2	HIS B 208	-14.330	6.707	17.418	1.00	6.76
35	ATOM	1563	ND1	HIS B 208	-15.239	7.175	19.346	1.00	7.15
	ATOM	1564	CE1	HIS B 208	-15.982	6.241	18.783	1.00	7.14
	ATOM	1565	NE2	HIS B 208	-15.452	5.939	17.613	1.00	7.63

	ATOM	1566	C	HIS B 208	-11.584	6.843	20.019	1.00	7.12
	ATOM	1567	O	HIS B 208	-10.643	6.792	19.181	1.00	5.72
	ATOM	1568	N	CYS B 209	-11.988	5.814	20.774	1.00	7.20
	ATOM	1569	CA	CYS B 209	-11.346	4.495	20.781	1.00	7.10
5	ATOM	1570	C	CYS B 209	-9.894	4.547	21.312	1.00	5.42
	ATOM	1571	O	CYS B 209	-9.070	3.681	20.990	1.00	4.32
	ATOM	1572	CB	CYS B 209	-11.412	3.857	19.385	1.00	8.32
	ATOM	1573	SG	CYS B 209	-13.091	3.602	18.713	1.00	10.94
	ATOM	1574	N	GLY B 210	-9.603	5.572	22.119	1.00	3.19
10	ATOM	1575	CA	GLY B 210	-8.283	5.758	22.712	1.00	2.87
	ATOM	1576	C	GLY B 210	-7.129	5.913	21.742	1.00	3.31
	ATOM	1577	O	GLY B 210	-5.973	5.573	22.061	1.00	7.40
	ATOM	1578	N	ILE B 211	-7.413	6.451	20.570	1.00	2.00
	ATOM	1579	CA	ILE B 211	-6.387	6.612	19.553	1.00	2.00
15	ATOM	1580	CB	ILE B 211	-6.981	7.148	18.250	1.00	2.48
	ATOM	1581	CG2	ILE B 211	-7.504	8.578	18.437	1.00	3.27
	ATOM	1582	CG1	ILE B 211	-5.942	7.033	17.135	1.00	2.07
	ATOM	1583	CD1	ILE B 211	-6.495	7.020	15.792	1.00	2.62
	ATOM	1584	C	ILE B 211	-5.176	7.433	19.990	1.00	3.39
20	ATOM	1585	O	ILE B 211	-4.064	7.203	19.523	1.00	4.21
	ATOM	1586	N	ALA B 212	-5.360	8.324	20.951	1.00	2.80
	ATOM	1587	CA	ALA B 212	-4.253	9.142	21.433	1.00	3.27
	ATOM	1588	CB	ALA B 212	-4.661	10.618	21.437	1.00	4.12
	ATOM	1589	C	ALA B 212	-3.760	8.726	22.822	1.00	2.81
25	ATOM	1590	O	ALA B 212	-2.908	9.402	23.394	1.00	3.98
	ATOM	1591	N	SER B 213	-4.253	7.603	23.346	1.00	2.50
	ATOM	1592	CA	SER B 213	-3.869	7.141	24.685	1.00	3.65
	ATOM	1593	CB	SER B 213	-4.984	6.284	25.313	1.00	4.01
	ATOM	1594	OG	SER B 213	-6.229	6.976	25.350	1.00	5.80
30	ATOM	1595	C	SER B 213	-2.532	6.404	24.800	1.00	2.77
	ATOM	1596	O	SER B 213	-1.979	6.311	25.886	1.00	5.92
	ATOM	1597	N	ALA B 214	-2.043	5.849	23.696	1.00	6.22
	ATOM	1598	CA	ALA B 214	-0.775	5.122	23.680	1.00	6.26
	ATOM	1599	CB	ALA B 214	-0.996	3.633	23.957	1.00	6.33
35	ATOM	1600	C	ALA B 214	-0.116	5.315	22.327	1.00	5.15
	ATOM	1601	O	ALA B 214	0.117	4.349	21.591	1.00	5.92
	ATOM	1602	N	ALA B 215	0.154	6.573	21.985	1.00	3.16

	ATOM	1603	CA	ALA B 215	0.780	6.901	20.707	1.00	3.49
	ATOM	1604	CB	ALA B 215	0.124	8.189	20.091	1.00	2.00
	ATOM	1605	C	ALA B 215	2.289	7.085	20.886	1.00	3.15
	ATOM	1606	O	ALA B 215	2.754	7.576	21.931	1.00	3.84
5	ATOM	1607	N	SER B 216	3.056	6.680	19.882	1.00	2.80
	ATOM	1608	CA	SER B 216	4.510	6.800	19.943	1.00	2.95
	ATOM	1609	CB	SER B 216	5.080	5.835	20.992	1.00	5.18
	ATOM	1610	OG	SER B 216	4.914	4.487	20.572	1.00	6.13
	ATOM	1611	C	SER B 216	5.152	6.525	18.575	1.00	3.03
10	ATOM	1612	O	SER B 216	4.490	6.051	17.640	1.00	3.02
	ATOM	1613	N	TYR B 217	6.437	6.855	18.469	1.00	3.25
	ATOM	1614	CA	TYR B 217	7.214	6.644	17.251	1.00	3.81
	ATOM	1615	CB	TYR B 217	7.101	7.853	16.297	1.00	4.94
	ATOM	1616	CG	TYR B 217	7.657	9.164	16.829	1.00	5.35
15	ATOM	1617	CD1	TYR B 217	8.954	9.559	16.536	1.00	5.88
	ATOM	1618	CE1	TYR B 217	9.455	10.791	16.955	1.00	6.10
	ATOM	1619	CD2	TYR B 217	6.865	10.036	17.568	1.00	6.74
	ATOM	1620	CE2	TYR B 217	7.360	11.284	17.994	1.00	7.90
	ATOM	1621	CZ	TYR B 217	8.657	11.646	17.676	1.00	7.27
20	ATOM	1622	OH	TYR B 217	9.153	12.865	18.075	1.00	9.53
	ATOM	1623	C	TYR B 217	8.677	6.400	17.662	1.00	3.37
	ATOM	1624	O	TYR B 217	9.079	6.757	18.777	1.00	2.04
	ATOM	1625	N	PRO B 218	9.475	5.746	16.791	1.00	5.38
	ATOM	1626	CD	PRO B 218	9.086	4.997	15.572	1.00	2.00
25	ATOM	1627	CA	PRO B 218	10.883	5.489	17.136	1.00	4.81
	ATOM	1628	CB	PRO B 218	11.204	4.223	16.329	1.00	2.00
	ATOM	1629	CG	PRO B 218	10.419	4.417	15.094	1.00	2.00
	ATOM	1630	C	PRO B 218	11.810	6.669	16.763	1.00	5.05
	ATOM	1631	O	PRO B 218	11.553	7.366	15.791	1.00	5.60
30	ATOM	1632	N	THR B 219	12.831	6.929	17.579	1.00	6.63
	ATOM	1633	CA	THR B 219	13.781	8.005	17.297	1.00	9.58
	ATOM	1634	CB	THR B 219	14.396	8.645	18.582	1.00	10.22
	ATOM	1635	OG1	THR B 219	15.062	7.652	19.366	1.00	11.19
	ATOM	1636	CG2	THR B 219	13.320	9.293	19.434	1.00	10.92
35	ATOM	1637	C	THR B 219	14.888	7.429	16.438	1.00	11.99
	ATOM	1638	O	THR B 219	15.419	6.350	16.714	1.00	11.40
	ATOM	1639	N	VAL B 220	15.191	8.101	15.344	1.00	15.02

ATOM	1640	CA	VAL B 220	16.235	7.625	14.466	1.00	16.04
ATOM	1641	CB	VAL B 220	15.672	7.471	13.031	1.00	16.05
ATOM	1642	CG1	VAL B 220	16.733	7.103	12.089	1.00	17.27
ATOM	1643	CG2	VAL B 220	14.637	6.353	13.010	1.00	14.61
5 ATOM	1644	C	VAL B 220	17.454	8.570	14.599	1.00	19.22
ATOM	1645	O	VAL B 220	18.620	8.098	14.498	1.00	21.47
ATOM	1646	OH	VAL B 220	17.243	9.755	14.954	1.00	18.51
ATOM	1647	OH2	WAT C 400	1.715	-0.341	10.220	1.00	4.25
ATOM	1648	OH2	WAT C 401	7.097	7.224	11.030	1.00	2.00
10 ATOM	1649	OH2	WAT C 402	-10.695	7.378	16.639	1.00	5.94
ATOM	1650	OH2	WAT C 403	2.737	3.013	20.821	1.00	5.69
ATOM	1651	OH2	WAT C 404	4.712	-2.112	7.932	1.00	4.54
ATOM	1652	OH2	WAT C 405	-0.335	-2.968	7.131	1.00	2.00
ATOM	1653	OH2	WAT C 406	-13.889	-1.040	17.915	1.00	3.20
15 ATOM	1654	OH2	WAT C 407	-5.874	17.220	22.788	1.00	7.23
ATOM	1655	OH2	WAT C 408	-8.649	16.659	11.052	1.00	7.00
ATOM	1656	OH2	WAT C 409	5.217	4.237	7.361	1.00	2.00
ATOM	1657	OH2	WAT C 410	4.460	1.690	6.263	1.00	2.45
ATOM	1658	OH2	WAT C 411	12.655	9.649	14.739	1.00	10.53
20 ATOM	1659	OH2	WAT C 412	17.802	-10.437	17.933	1.00	9.17
ATOM	1660	OH2	WAT C 413	-17.578	-5.887	21.444	1.00	8.88
ATOM	1661	OH2	WAT C 414	-3.197	5.183	20.980	1.00	7.65
ATOM	1662	OH2	WAT C 415	-5.965	-3.631	6.935	1.00	5.92
ATOM	1663	OH2	WAT C 416	12.786	1.123	6.736	1.00	5.33
25 ATOM	1664	OH2	WAT C 417	3.012	16.347	20.074	1.00	6.15
ATOM	1665	OH2	WAT C 418	-6.541	17.076	17.084	1.00	4.69
ATOM	1666	OH2	WAT C 419	8.324	-10.560	8.482	1.00	4.57
ATOM	1667	OH2	WAT C 420	-15.621	-11.150	15.846	1.00	12.03
ATOM	1668	OH2	WAT C 421	-11.693	11.210	18.286	1.00	2.91
30 ATOM	1669	OH2	WAT C 422	-0.401	8.726	24.177	1.00	8.52
ATOM	1670	OH2	WAT C 423	-0.681	-0.811	11.002	1.00	2.50
ATOM	1671	OH2	WAT C 424	2.152	-1.861	7.987	1.00	7.69
ATOM	1672	OH2	WAT C 425	10.844	-17.495	11.881	1.00	24.05
ATOM	1673	OH2	WAT C 426	4.113	6.208	0.742	1.00	9.50
35 ATOM	1674	OH2	WAT C 427	-0.361	18.287	4.743	1.00	21.23
ATOM	1675	OH2	WAT C 428	-2.237	20.526	17.810	1.00	16.66
ATOM	1676	OH2	WAT C 429	-19.138	-6.191	19.225	1.00	7.57

	ATOM	1677	OH2	WAT	C	430	19.473	-14.562	15.685	1.00	11.49
	ATOM	1678	OH2	WAT	C	431	-1.376	-2.848	12.708	1.00	3.21
	ATOM	1679	OH2	WAT	C	432	3.284	3.606	24.573	1.00	9.31
	ATOM	1680	OH2	WAT	C	433	-14.786	15.166	14.179	1.00	14.71
5	ATOM	1681	OH2	WAT	C	434	12.094	-5.678	2.193	1.00	11.37
	ATOM	1682	OH2	WAT	C	435	6.466	-11.420	4.246	1.00	6.71
	ATOM	1683	OH2	WAT	C	436	22.706	-5.931	15.160	1.00	8.12
	ATOM	1684	OH2	WAT	C	437	-8.611	19.110	10.002	1.00	9.78
	ATOM	1685	OH2	WAT	C	438	0.738	15.034	3.641	1.00	20.62
10	ATOM	1686	OH2	WAT	C	439	4.124	-9.086	6.384	1.00	14.29
	ATOM	1687	OH2	WAT	C	440	-13.887	-3.607	2.668	1.00	13.17
	ATOM	1688	OH2	WAT	C	441	-7.572	14.126	23.703	1.00	18.38
	ATOM	1689	OH2	WAT	C	442	0.874	7.459	26.362	1.00	22.12
	ATOM	1690	OH2	WAT	C	443	9.305	-14.700	20.411	1.00	20.46
15	ATOM	1691	OH2	WAT	C	444	-8.955	15.927	4.448	1.00	25.82
	ATOM	1692	OH2	WAT	C	445	11.930	-13.702	21.523	1.00	10.86
	ATOM	1693	OH2	WAT	C	446	3.469	-16.357	23.297	1.00	19.39
	ATOM	1694	OH2	WAT	C	447	11.878	3.079	5.063	1.00	8.26
	ATOM	1695	OH2	WAT	C	448	-3.082	3.376	0.174	1.00	11.22
20	ATOM	1696	OH2	WAT	C	449	-4.375	0.291	0.313	1.00	7.70
	ATOM	1697	OH2	WAT	C	450	4.771	14.939	-2.264	1.00	11.11
	ATOM	1698	OH2	WAT	C	451	15.349	1.340	6.121	1.00	14.46
	ATOM	1699	OH2	WAT	C	452	-0.319	1.922	2.215	1.00	6.91
	ATOM	1700	OH2	WAT	C	453	15.061	-15.434	4.049	1.00	21.29
25	ATOM	1701	OH2	WAT	C	454	-15.574	9.174	21.509	1.00	19.68
	ATOM	1702	OH2	WAT	C	455	-5.683	-18.497	22.276	1.00	7.98
	ATOM	1703	OH2	WAT	C	456	16.054	3.526	4.535	1.00	15.78
	ATOM	1704	OH2	WAT	C	457	1.796	-9.826	5.952	1.00	15.52
	ATOM	1705	OH2	WAT	C	458	7.900	-11.446	20.651	1.00	9.56
30	ATOM	1706	OH2	WAT	C	459	-15.694	12.658	13.651	1.00	15.95
	ATOM	1707	OH2	WAT	C	460	-18.800	4.491	8.685	1.00	30.26
	ATOM	1708	OH2	WAT	C	461	3.842	-3.870	2.301	1.00	5.98
	ATOM	1709	OH2	WAT	C	462	-1.911	-0.828	-0.023	1.00	11.85
	ATOM	1710	OH2	WAT	C	463	-19.071	4.290	11.811	1.00	9.95
35	ATOM	1711	OH2	WAT	C	464	-10.861	-2.452	0.116	1.00	19.11
	ATOM	1712	OH2	WAT	C	465	-9.801	14.751	22.263	1.00	15.42
	ATOM	1713	OH2	WAT	C	466	-7.905	6.223	1.616	1.00	30.93

	ATOM	1714	OH2	WAT	C	467	18.856	4.715	11.980	1.00	10.43
	ATOM	1715	OH2	WAT	C	468	4.553	17.830	24.004	1.00	19.36
	ATOM	1716	OH2	WAT	C	469	-22.103	-6.169	18.782	1.00	26.20
	ATOM	1717	OH2	WAT	C	470	22.883	-2.193	20.022	1.00	27.05
5	ATOM	1718	OH2	WAT	C	471	-8.283	18.361	22.060	1.00	14.94
	ATOM	1719	OH2	WAT	C	472	-19.067	-4.655	23.491	1.00	12.52
	ATOM	1720	OH2	WAT	C	473	-25.358	3.482	20.935	1.00	18.60
	ATOM	1721	OH2	WAT	C	474	3.113	1.129	25.678	1.00	16.37
	ATOM	1722	OH2	WAT	C	475	-14.114	19.680	-0.525	1.00	19.49
10	ATOM	1723	OH2	WAT	C	476	7.483	15.405	-1.684	1.00	20.28
	ATOM	1724	OH2	WAT	C	477	2.890	14.130	29.288	1.00	22.65
	ATOM	1725	OH2	WAT	C	478	-24.545	-8.477	18.440	1.00	22.79
	ATOM	1726	OH2	WAT	C	479	23.711	-7.909	16.612	1.00	26.08
	ATOM	1727	OH2	WAT	C	480	11.306	4.954	-1.712	1.00	18.71
15	ATOM	1728	OH2	WAT	C	481	13.249	5.572	24.427	1.00	11.66
	ATOM	1729	OH2	WAT	C	482	14.941	3.560	24.925	1.00	18.00
	ATOM	1730	OH2	WAT	C	483	19.849	9.786	12.745	1.00	21.86
	ATOM	1731	OH2	WAT	C	484	-7.714	15.740	26.319	1.00	19.77
	ATOM	1732	OH2	WAT	C	485	18.128	-14.939	19.458	1.00	17.22
20	ATOM	1733	OH2	WAT	C	486	-21.893	-4.075	14.601	1.00	21.40
	ATOM	1734	OH2	WAT	C	487	-2.211	22.607	20.592	1.00	27.68
	ATOM	1735	OH2	WAT	C	488	-9.940	17.323	20.067	1.00	15.74
	ATOM	1736	OH2	WAT	C	489	2.969	17.859	7.635	1.00	17.12
	ATOM	1737	OH2	WAT	C	490	-7.798	-7.724	-4.389	1.00	13.80
25	ATOM	1738	OH2	WAT	C	491	21.839	-2.359	11.757	1.00	21.04
	ATOM	1739	OH2	WAT	C	492	3.610	1.069	22.604	1.00	11.34
	ATOM	1740	OH2	WAT	C	493	10.695	-2.690	0.512	1.00	21.14
	ATOM	1741	OH2	WAT	C	494	15.726	-17.968	19.611	1.00	16.41
	ATOM	1742	OH2	WAT	C	495	18.038	-14.823	8.893	1.00	22.45
30	ATOM	1743	OH2	WAT	C	496	-19.607	-0.615	11.547	1.00	16.65
	ATOM	1744	OH2	WAT	C	497	2.915	15.247	5.332	1.00	15.60
	ATOM	1745	OH2	WAT	C	498	19.132	-12.808	17.530	1.00	13.34
	ATOM	1746	OH2	WAT	C	499	-2.344	-16.737	9.713	1.00	16.66
	ATOM	1747	OH2	WAT	C	500	-18.639	0.788	7.355	1.00	15.66
35	ATOM	1748	OH2	WAT	C	501	0.462	15.302	-2.725	1.00	14.82
	ATOM	1749	OH2	WAT	C	502	-7.398	20.029	12.052	1.00	26.98
	ATOM	1750	OH2	WAT	C	503	15.757	-11.340	29.166	1.00	11.53

	ATOM	1751	OH2	WAT	C	504	19.014	0.690	5.325	1.00	22.02
	ATOM	1752	OH2	WAT	C	505	16.120	-13.057	20.864	1.00	15.98
	ATOM	1753	OH2	WAT	C	506	-6.380	18.090	29.315	1.00	16.80
	ATOM	1754	OH2	WAT	C	507	14.293	-15.012	21.072	1.00	13.45
5	ATOM	1755	OH2	WAT	C	508	9.526	-19.735	19.933	1.00	21.58
	ATOM	1756	OH2	WAT	C	509	-12.325	16.124	21.846	1.00	20.83
	ATOM	1757	OH2	WAT	C	510	15.864	7.749	25.554	1.00	11.44
	ATOM	1758	OH2	WAT	C	511	20.012	-0.457	24.073	1.00	17.87
	ATOM	1759	OH2	WAT	C	512	2.459	6.458	24.433	1.00	20.00
10	ATOM	1760	OH2	WAT	C	513	-3.245	-7.574	17.264	1.00	20.00
	ATOM	1761	OH2	WAT	C	514	-2.009	-5.446	-5.665	1.00	20.00
	ATOM	1762	OH2	WAT	C	515	11.141	-3.191	26.733	1.00	20.00
	ATOM	1763	OH2	WAT	C	516	-1.734	-4.445	21.459	1.00	20.00
	ATOM	1764	OH2	WAT	C	517	-7.062	19.554	16.658	1.00	20.00
15	ATOM	1765	OH2	WAT	C	518	10.312	-0.626	26.447	1.00	20.00
	ATOM	1766	OH2	WAT	C	519	-12.539	-5.135	28.522	1.00	20.00
	ATOM	1767	OH2	WAT	C	520	17.357	-8.676	23.160	1.00	20.00
	ATOM	1768	OH2	WAT	C	521	1.704	17.298	-2.824	1.00	20.00
	ATOM	1769	OH2	WAT	C	522	-24.997	6.317	22.486	1.00	20.00
20	ATOM	1770	OH2	WAT	C	523	21.437	6.317	22.486	1.00	20.00
	ATOM	1771	OH2	WAT	C	524	11.336	16.240	9.222	1.00	20.00
	ATOM	1772	OH2	WAT	C	525	13.648	-3.524	28.036	1.00	20.00
	ATOM	1773	OH2	WAT	C	526	19.248	-10.257	26.167	1.00	20.00
	ATOM	1774	OH2	WAT	C	527	-22.056	-6.157	23.245	1.00	20.00
25	ATOM	1775	OH2	WAT	C	528	24.378	-6.157	23.245	1.00	20.00
	ATOM	1776	OH2	WAT	C	529	3.398	-16.519	20.213	1.00	20.00
	ATOM	1777	OH2	WAT	C	530	-0.867	-2.050	22.075	1.00	20.00
	ATOM	1778	OH2	WAT	C	531	13.363	-12.892	28.748	1.00	20.00
	ATOM	1779	OH2	WAT	C	532	15.134	-16.191	7.553	1.00	20.00
30	ATOM	1780	OH2	WAT	C	533	-2.778	-7.172	20.885	1.00	20.00
	ATOM	1781	OH2	WAT	C	534	-5.662	-6.615	-5.903	1.00	20.00
	ATOM	1782	OH2	WAT	C	535	18.366	2.686	3.326	1.00	20.00
	ATOM	1783	OH2	WAT	C	536	-1.839	15.842	-4.199	1.00	20.00
	ATOM	1784	OH2	WAT	C	537	8.606	5.745	-1.225	1.00	20.00
35	ATOM	1785	OH2	WAT	C	538	4.084	16.971	-1.150	1.00	20.00
	ATOM	1786	OH2	WAT	C	539	-9.310	-12.146	0.259	1.00	20.00
	ATOM	1787	OH2	WAT	C	540	-13.659	5.332	27.584	1.00	20.00

ATOM	1788	OH2	WAT	C	541	-13.793	20.379	9.540	1.00	20.00
ATOM	1789	OH2	WAT	C	542	-20.284	-3.453	17.374	1.00	20.00
ATOM	1790	OH2	WAT	C	543	9.337	13.701	8.362	1.00	20.00
ATOM	1791	OH2	WAT	C	544	-9.440	-10.243	-4.503	1.00	20.00
5 ATOM	1792	OH2	WAT	C	545	12.473	0.613	27.161	1.00	20.00
ATOM	1793	OH2	WAT	C	546	16.546	-17.419	8.428	1.00	20.00
ATOM	1794	OH2	WAT	C	547	-1.129	-4.481	-0.369	1.00	20.00
ATOM	1795	OH2	WAT	C	548	12.028	-16.285	22.590	1.00	20.00
ATOM	1796	OH2	WAT	C	549	-10.803	20.596	9.099	1.00	20.00
10 ATOM	1797	OH2	WAT	C	550	-21.302	6.052	25.675	1.00	20.00
ATOM	1798	OH2	WAT	C	551	20.665	2.849	18.416	1.00	20.00
ATOM	1799	OH2	WAT	C	552	8.171	-13.093	23.401	1.00	20.00
ATOM	1800	OH2	WAT	C	553	10.372	-2.692	29.515	1.00	20.00
ATOM	1801	OH2	WAT	C	554	10.863	-15.981	7.960	1.00	20.00
15 ATOM	1802	OH2	WAT	C	555	-2.252	-5.584	24.473	1.00	20.00
ATOM	1803	OH2	WAT	C	556	6.457	-5.032	2.210	1.00	20.00
ATOM	1804	OH2	WAT	C	557	-11.210	17.326	2.413	1.00	20.00
END										

20 Example 5

Assay of Inhibition of Cathepsin L Activity

Potential drugs may be tested for inhibition of Cathepsin L activity as follows.

- 25 Briefly, Cathepsin L (19 pM final as determined by active site titration using E-64, Barrett et al., 1981, Methods in Enzymology, 80: 535) is added to 750 μ L of assay buffer consisting of 340 nM sodium acetate - 60 mM acetic acid (pH 5.5), 4 mM disodium EDTA, and 8 mM DTT. Peptides were added at concentrations ranging from on to 35 μ M. After a 6 minute incubation at 25°C, 1500 uL of 0.1% Brij 35 was added and the reaction
- 30 started with 5.0 μ M Z-Phe-Arg-NMec(AMC) (AMC is aminomethylcoumarin). The fluorescence of the free aminomethylcoumarin is measured in a fluorimeter at excitation of 370 nm and an emission at 432 nm over a 6 minute time period. Fluorescence was converted to μ M AMC released by using a standard curve generated by plotting μ M AMC vs. fluorescence, and plotted vs. time. In order to calculate the velocities, a linear least
- 35 squares analysis is performed over the initial part of the data. The IC₅₀ values are

determined from Dixon plots of the form V/V_0 (velocity without compound/velocity with compound) vs. compound concentration.

Example 6

5 Assay of inhibition of proteoglycan degradation

Cathepsins B and L have been found to degrade cartilage components, causing the degradation of associated proteoglycans (Maciewicz and Wotton, *Biomedica Biochimica Acta*, 50, 561-4, 1991). Previous results by the same researchers indicated that these
10 enzymes are found in active form in the synovial fluid of arthritic patients. The conclusion drawn was that cysteine proteinases play a role in the etiology of arthritis.

Cartilage degradation can be induced by the *in vivo* injection of IL-1 into the joint capsule of rabbits, and the administration of a large serine protease inhibitor PN-1 (43 KD) can ameliorate this degradation (Stevens et al., *Agents and Actions, Supplements*, 39, 173-
15 7, 1993). It has been found that low molecular weight synthetic peptide metalloproteinase inhibitor can prevent the breakdown of proteoglycan within articular cartilage *in vitro*. (Andrews et al., *Agents and Actions*, 37, 147-54, 1992). Certain cysteine endopeptidase inactivators were found to inhibit IL-1 stimulated structural cartilage proteoglycan degradation. E64 and Ep475, broad-spectrum cysteine protease inhibitors) did not work at
20 100 μ M concentrations. However lipophilic derivatives inhibited at 10 μ M to 1 μ M concentrations. (Buttle et al., *Biochemical Journal*, 281, 175-7, 1992). Compounds can be tested for the ability to inhibit articular cartilage proteoglycan degradation, as measured by proteoglycan release after IL-1 stimulation.

The assay system used for testing the peptides for inhibitory activity of
25 proteoglycan release is a micro organ culture assay (MOCA). Papain; cetyl pyridinium chloride and chondroitin sulfate type C is purchased from Sigma Chemical Co. (St. Louis, MO). Interleukin 1 alpha is purchased from Collaborative Research. ABCase, chondroitinase, ABC lyase, and keratanase is obtained from ICI. $\text{Na}^{35}\text{SO}_4$ is purchased from NEN.

30 Articular cartilage explants from calf knee joints are maintained in culture in DMEM medium containing 20 μ Ci/ml $\text{Na}^{35}\text{SO}_4$ for 48 hours for the incorporation of label

into newly synthesized proteoglycan (PG). The radiolabelled medium is then removed, the radiolabelled explants washed 3 x 30 ml cold DMEM and placed into a 96 well plate with or without IL-1 (Interleukin-1 alpha, 50 U/ml) and various concentrations of test compound. The explants are incubated first for 24 hours in the presence of IL-1 in order to
5 ensure initiation of IL-1 induced auto-catalysis prior to the addition of various metalloprotease inhibitors for an additional 72 hours.

The newly synthesized radiolabelled proteoglycans released during the cultivation period are subjected to enzymatic digestion with papain. Briefly, an aliquot of 150 µl of medium from the original culture volume (300 µl) was incubated with 100 µl of papain
10 (3 ml/ml) for 2 hours at 65°C. A 50 µl aliquot of the papain digested material containing radiolabelled $^{35}\text{SO}_4$ -gag (glycosaminoglycans, mucopolysaccharide) is incubated with 100 µl of cetylpyridinium chloride (cpc, 4% cpc + 40 nM NaSO_4) plus cold chondroitin sulfate standard (30 µl of 2.5 mg/ml solution). The samples are placed on ice for 60 minutes, and the radiolabelled gags are precipitated and collected on a 96 well plate
15 harvester (MACH2, TOMTEC, Orange, CT) glass fiber filter. The filter is dried and counted after addition of 10 mls of scintillation cocktail (scintillant).

SEQUENCE LISTING

(1) GENERAL INFORMATION:

5

(i) APPLICANT:

- (A) NAME: Zeneca Limited
- (B) STREET: 15 Stanhope Gate
- (C) CITY: London
- (E) COUNTRY: United Kingdom
- (F) POSTAL CODE (ZIP): W1Y 6LN
- (G) TELEPHONE: (0171) 304 5000
- (H) TELEFAX: (0171) 304 5151

10

15

(ii) TITLE OF INVENTION: Protein

(iii) NUMBER OF SEQUENCES: 8

(iv) COMPUTER READABLE FORM:

20

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

25

(vi) PRIOR APPLICATION DATA:

- (A) APPLICATION NUMBER: GB 9522660.1
- (B) FILING DATE: 04-NOV-1995

30 (2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: other nucleic acid

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GCAGTAAGAT ATGAATCCTA CACT

24

5 (2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 base pairs

(B) TYPE: nucleic acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

20 CATCACCGTC CACAGCTCAC ACAG

24

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 33 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: other nucleic acid

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GATGACCATG GCGACTCTAA CATTGATCA CAG

33

(2) INFORMATION FOR SEQ ID NO: 4:

40

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: other nucleic acid

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

CTGCCTGAAT TCTTCACTGG TCATGTCTC

29

(2) INFORMATION FOR SEQ ID NO: 5:

15

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: other nucleic acid

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CTATCCATAT GAGGCAACAG AAGAATCCTG

30

30

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: other nucleic acid

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

GACAAGCTTG AATTCTTATT AGTGATGGTG ATGGTGGTGC ACAGTGGGGT AGCTGGCTG 59
5

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1575 base pairs
10 (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

20 AGAACCGCGA CCTCCGCAAC CTTGAGCGGC ATCCGTGGAG TGGCCTGCA GCTACGACCG 60
CAGCAGGAAA GCGCCGCCGG CCAGGCCAG CTGTGGCCGG ACAGGACTG GAAGAGAGGA 120
25 CGCGGTGAG TAGGTGTGCA CCAGCCCTGG CAACGAGAGC GTCTACCCCG AACTCTGCTG 180
GCCTTGAGGT GGGGAAGCCG GGGAGGGCAG TTGAGGACCC CGCGGAGGCG CGTGA CTGGT 240
TGAGCGGGCA GGCCAGCCTC CGAGCCGGGT GGACACAGGT TTTAAAACAT GAATCCTACA 300
30 CTCATCCTTG CTGCCTTTTG CCTGGGAATT GCCTCAGCTA CTCTAACATT TGATCAGAGT 360
TTAGAGGCAC AGTGGACCAA GTGGAAGGCG ATGCACAACA GATTATACGG CATGAATGAA 420
35 GAAGGATGGA GGAGAGCAGT GTGGGAGAAG AACATGAAGA TGATTGAACT GCACAATCAG 480
GAATACAGGG AAGGGAAACA CAGCTTCACA ATGGCCATGA ACGCCTTTGG AGACATGACC 540
AGTGAAGAAT TCAGGCAGGT GATGAATGGC TTTCAAACCC GTAAGCCCAG GAAGGGGAAA 600
40 GTGTTCCAGG AACCTCTGTT TTATGAGGCC CCCAGATCTG TGGATTGGAG AGAGAAAGGC 660

	TACGTGACTC CTGTGAAGAA TCAGGGTCAG TGTGGTTCTT GTTGGGCTTT TAGTGCTACT	720
	GGTGCTCTTG AAGGACAGAT GTTCCGAAA ACTGGGAGGC TTATCTCACT GAGTGAGCAG	780
5	AATCTGGTAG ACTGCTCTGG GCCTCAAGGC AATGAAGGCT GCAATGGTGG CCTAATGGAT	840
	TATGCTTTCC AGTATGTTCA GGATAATGGA GGCCTGGACT CTGAGGAATC CTATCCATAT	900
	GAGGCAACAG AAGAATCCTG TAAGTACAAT CCCAAGTATT CTGTTGCTAA TGACACCGGC	960
10	TTTGTGGACA TCCCTAAGCA GGAGAAGGCC CTGATGAAGG CAGTTGCAAC TGTGGGGCCC	1020
	ATTTCTGTTG CTATTGATGC AGGTCATGAG TCCTTCCTGT TCTATAAAGA AGGCATTTAT	1080
15	TTTGAGCCAG ACTGTAGCAG TGAAGACATG GATCATGGTG TGCTGGTGGT TGGCTACGGA	1140
	TTTGAAAGCA CAGAATCAGA TAACAATAAA TATTGGCTGG TGAAGAACAG CTGGGGTGAA	1200
	GAATGGGGCA TGGGTGGCTA CGTAAAGATG GCCAAAGACC GGAGAAACCA TTGTGGAATT	1260
20	GCCTCAGCAG CCAGCTACCC CACTGTGTGA GCTGGTGGAC GGTGATGAGG AAGGACTTGA	1320
	CTGGGGATGG CGCATGCATG GGAGGAATTC ATCTTCAGTC TACCAGCCCC CGCTGTGTCTG	1380
25	GATACACACT CGAATCATTG AAGATCCGAG TGTGATTGTA ATTCTGTGAT ATTTTCACAC	1440
	TGGTAAATGT TACCTCTATT TTAATTACTG CTATAAATAG GTTTATATTA TTGATTCACT	1500
	TACTGACTTT GCATTTTCGT TTTTAAAGG ATGTATAAAT TTTTACCTGT TTAAATAAAA	1560
30	TTTAATTTCA AATGT	1575

(2) INFORMATION FOR SEQ ID NO: 8:

- 35 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 333 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- 40 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

5	Met Asn Pro Thr Leu Ile Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser	1	5	10	15
	Ala Thr Leu Thr Phe Asp His Ser Leu Glu Ala Gln Trp Thr Lys Trp	20	25	30	
10	Lys Ala Met His Asn Arg Leu Tyr Gly Met Asn Glu Glu Gly Trp Arg	35	40	45	
	Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gln	50	55	60	
15	Glu Tyr Arg Glu Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe	65	70	75	80
	Gly Asp Met Thr Ser Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln	85	90	95	
20	Asn Arg Lys Pro Arg Lys Gly Lys Val Phe Gln Glu Pro Leu Phe Tyr	100	105	110	
	Glu Ala Pro Arg Ser Val Asp Trp Arg Glu Lys Gly Tyr Val Thr Pro	115	120	125	
25	Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr	130	135	140	
	Gly Ala Leu Glu Gly Gln Met Phe Arg Lys Thr Gly Arg Leu Ile Ser	145	150	155	160
30	Leu Ser Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu	165	170	175	
35	Gly Cys Asn Gly Gly Leu Met Asp Tyr Ala Phe Gln Tyr Val Gln Asp	180	185	190	
	Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu	195	200	205	
40	Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly				

	210	215	220
	Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala		
	225	230	235 240
5	Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe		
	245	250	255
	Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu		
10	260	265	270
	Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr		
	275	280	285
15	Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu		
	290	295	300
	Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn		
	305	310	315 320
20	His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val		
	325	330	

CLAIMS

1. Cathepsin L at a specific activity of at least 40,000 nmoles/min/mg.
2. Cathepsin L at a specific activity of at least 100,000 nmoles/min/mg.
- 5 3. Cathepsin L in crystalline form.
4. Cathepsin L according to claim 3 in which the crystals possess a monoclinic space group $P2_1$, with unit cell dimensions $a = 46.23$, $b = 49.38$, $c = 49.25$ Å and $\beta = 113.45^\circ$.
5. Cathepsin L according to claim 4 in which the crystals are wedge-shaped crystals having the atomic coordinates set out in Example 4.
- 10 6. A secretion vector for directed inducible expression of cathepsin L into the periplasm of *E.coli*.
7. An *E.coli* host comprising a secretion vector for directed inducible expression of cathepsin L into the host periplasm.
8. A method of making cathepsin L which comprises culture of an *E.coli* host as
15 defined in claim 7 in a growth medium and optionally soluble cathepsin L is collected from the growth medium.
9. A method of making cathepsin L according to claim 8 in which the *E.coli* host is cultured at a temperature of 15-30°C.
10. A method of making cathepsin L according to claim 8 in which the *E.coli* host is
20 cultured at a temperature of about 25°C.
11. A method of making cathepsin L according to claim 8 in which the *E.coli* host is cultured at a temperature of about 25°C in the presence of a concentration of inducer optimised for maximal soluble expression of cathepsin.
12. *E. coli* MSD 2148 (MSD 213 pZen 1677) deposited under NCIMB accession no
25 40773.
13. The X-ray coordinates of cathepsin L as defined in Example 4.
14. The X-ray coordinates of the active site of cathepsin L as defined in Example 4 in residues 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189 & 209-214.
15. A method of rational drug design using a 3-dimensional structure of cathepsin L as
30 determined from X-ray diffraction data which comprises any of the following:

searching real and virtual compound databases for potential drugs; computational growth of potential ligands in the active site; or collecting X-ray diffraction data from crystals comprising potential drug.

16. A novel inhibitor of cathepsin L determined by rational drug design according to
5 the method of claim 15.

10 EC70116

AFG/MB : 10OCT96



Application No: GB 9622436.5
Claims searched: 1 to 16

Examiner: Mr S J Pilling
Date of search: 17 February 1997

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK CI (Ed.O): C3H (HB7E)

Int CI (Ed.6): C12N 9/64

Other: ONLINE: WPI, DIALOG/BIOTECH

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
X	Biol. Chem. Hoppe-Seyler, Vol. 376, June 1995, M Dolinar <i>et al</i> , "Expression of full length human procathepsin L cDNA in Escherichia coli and refolding of the expression product" pages 385 to 388, particularly page 387.	
X	Biosci. Biotech. Biochem., Vol. 57, No. 9, 1993, J J Lee <i>et al</i> "Purification and characterization of proteinases identified as cathepsins L and L-like (58 kDa) proteinase from mackerel (<i>Scomber australasicus</i>)", pages 1470 to 1476, particularly Table 1 on page 1473.	
X	Febs Letters, Vol. 336, No. 3, 1993, T Ogrinc <i>et al</i> , "Purification of the complex of Cathepsin l and the MHC class II-associated invariant chain fragment from human kidney", pages 555 to 559, particularly the results and discussion.	
X	Journal of Chromatography, Vol. 568, No. 1, 1991, V Dalet-Fumeron <i>et al</i> , "High performance liquid chromatographic method for the simultaneous purification of cathepsins B, H and L from human liver", pages 55 to 68, particularly the results.	
X	Comp. Biochem. Physiol., Vol. 96B, No. 2, 1990, M Yamashita & S Konagaya, "Purification and characterization of cathepsin L from the white muscle of Chum salmon, <i>Oncorhynchus keta</i> ", pages 247 to 252, particularly Table 1 on page 248.	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
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Claims searched: 1 to 16

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Category	Identity of document and relevant passage	Relevant to claims
X	J. Biochem., Vol 87, No. 4, 1980, (Tokyo) A Okitana <i>et al</i> , "Purification and some properties of a myofibrillar protein-degrading protease cathepsin L, from rabbit skeletal muscle", pages 1133 to 1143, particularly Table 1 on page 1139.	

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